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(34) **G-CSF analog compositions and methods.**

(37) Provided herein are granulocyte colony stimulating factor ("G-CSF") analogs, compositions containing such analogs, and related compositions. In another aspect, provided herein are nucleic acids encoding the present analogs or related nucleic acids, related host cells and vectors. In yet another aspect, provided herein are computer programs and apparatuses for expressing the three dimensional structure of G-CSF and analogs thereof. In another aspect, provided herein are methods for rationally designing G-CSF analogs and related compositions. In yet another aspect, provided herein are methods for treatment using the present G-CSF analogs.

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Field of the Invention

This invention relates to granulocyte colony stimulating factor ("G-CSF") analogs, compositions containing such analogs, and related compositions. In another aspect, the present invention relates to nucleic acids encoding the present analogs or related nucleic acids, related host cells and vectors. In another aspect, the invention relates to computer programs and apparatuses for expressing the three dimensional structure of G-CSF and analogs thereof. In another aspect, the invention relates to methods for rationally designing G-CSF analogs and related compositions. In yet another aspect, the present invention relates to methods for treatment using the present G-CSF analogs.

Background

Hematopoiesis is controlled by two systems: the cells within the bone marrow microenvironment and growth factors. The growth factors, also called colony stimulating factors, stimulate committed progenitor cells to proliferate and to form colonies of differentiating blood cells. One of these factors is granulocyte colony stimulating factor, herein called G-CSF, which preferentially stimulates the growth and development of neutrophils, indicating a potential use in neutropenic states. Welte et al., *PNAS-USA* 82: 1526-1530 (1985); Souza et al., *Science* 232: 61-65 (1986) and Gabrilove, J. *Seminars in Hematology* 26: (2) 1-14 (1989).

In humans, endogenous G-CSF is detectable in blood plasma. Jones et al., *Bailliere's Clinical Hematology* 2 (1): 83-111 (1989). G-CSF is produced by fibroblasts, macrophages, T cells trophoblasts, endothelial cells and epithelial cells and is the expression product of a single copy gene comprised of four exons and five introns located on chromosome seventeen. Transcription of this locus produces a mRNA species which is differentially processed, resulting in two forms of G-CSF mRNA, one version coding for a protein of 177 amino acids, the other coding for a protein of 174 amino acids, Nagata et al., *EMBO J* 5: 575-581 (1986), and the form comprised of 174 amino acids has been found to have the greatest specific *in vivo* biological activity. G-CSF is species cross-reactive, such that when human G-CSF is administered to another mammal such as a mouse, canine or monkey, sustained neutrophil leukocytosis is elicited. Moore et al., *PNAS-USA* 84: 7134-7138 (1987).

Human G-CSF can be obtained and purified from a number of sources. Natural human G-CSF (rhG-CSF) can be isolated from the supernatants of cultured human tumor cell lines. The development of recombinant DNA technology, see, for instance, U.S. Patent 4,810,643 (Souza) incorporated herein by reference, has enabled the production of commercial scale quantities of G-CSF in glycosylated form as a product of eukaryotic host cell expression, and of G-CSF in non-glycosylated form as a product of prokaryotic host cell expression.

G-CSF has been found to be useful in the treatment of indications where an increase in neutrophils will provide benefits. For example, for cancer patients, G-CSF is beneficial as a means of selectively stimulating neutrophil production to compensate for hematopoietic deficits resulting from chemotherapy or radiation therapy. Other indications include treatment of various infectious diseases and related conditions, such as sepsis, which is typically caused by a metabolite of bacteria. G-CSF is also useful alone, or in combination with other compounds, such as other cytokines, for growth or expansion of cells in culture, for example, for bone marrow transplants.

Signal transduction, the way in which G-CSF effects cellular metabolism, is not currently thoroughly understood. G-CSF binds to a cell-surface receptor which apparently initiates the changes within particular progenitor cells, leading to cell differentiation.

Various altered G-CSFs have been reported. Generally, for design of drugs, certain changes are known to have certain structural effects. For example, deleting one cysteine could result in the unfolding of a molecule which is, in its unaltered state, is normally folded via a disulfide bridge. There are other known methods for adding, deleting or substituting amino acids in order to change the function of a protein.

Recombinant human G-CSF mutants have been prepared, but the method of preparation does not include overall structure/function relationship information. For example, the mutation and biochemical modification of Cys 18 has been reported. Kuga et al., *Biochem. Biophys. Res. Comm* 159: 103-111 (1989); Lu et al., *Arch. Biochem. Biophys.* 268: 81-92 (1989).

In U.S. Patent No. 4, 810, 643, entitled, "Production of Pluripotent Granulocyte Colony-Stimulating Factor" (as cited above), polypeptide analogs and peptide fragments of G-CSF are disclosed generally. Specific G-CSF analogs disclosed include those with the cysteines at positions 17, 36, 42, 64, and 74 (of the 174 amino acid species or of those having 175 amino acids, the additional amino acid being an N-terminal methionine) substituted with another amino acid, (such as serine), and G-CSF with an alanine in the first (N-

terminal) position.

EP 0 335 423 entitled "Modified human G-CSF" reportedly discloses the modification of at least one amino group in a polypeptide having hG-CSF activity.

EP 0 272 703 entitled "Novel Polypeptide" reportedly discloses G-CSF derivatives having an amino acid substituted or deleted at or "in the neighborhood" of the N terminus.

EP 0 459 630, entitled "Polypeptides" reportedly discloses derivatives of naturally occurring G-CSF having at least one of the biological properties of naturally occurring G-CSF and a solution stability of at least 35% at 5 mg/ml in which the derivative has at least Cys¹⁷ of the native sequence replaced by a Ser¹⁷ residue and Asp²⁷ of the native sequence replaced by a Ser²⁷ residue.

EP 0 256 843 entitled "Expression of G-CSF and Muteins Thereof and Their Uses" reportedly discloses a modified DNA sequence encoding G-CSF wherein the N-terminus is modified for enhanced expression of protein in recombinant host cells, without changing the amino acid sequence of the protein.

EP 0 243 153 entitled "Human G-CSF Protein Expression" reportedly discloses G-CSF to be modified by inactivating at least one yeast KEX2 protease processing site for increased yield in recombinant production using yeast.

Shaw, U.S. Patent No. 4,904,584, entitled "Site-Specific Homogeneous Modification of Polypeptides," reportedly discloses lysine altered proteins.

WO/9012874 reportedly discloses cysteine altered variants of proteins.

Australian patent application Document No. AU-A-10948/92, entitled, "Improved Activation of Recombinant Proteins" reportedly discloses the addition of amino acids to either terminus of a G-CSF molecule for the purpose of aiding in the folding of the molecule after prokaryotic expression.

Australian patent application Document No. AU-A-76380/91, entitled, "Muteins of the Granulocyte Colony Stimulating Factor (G-CSF)" reportedly discloses muteins of the granulocyte stimulating factor G-CSF in the sequence Leu-Gly-His-Ser-Leu-Gly-Ile at position 50-56 of G-CSF with 174 amino acids, and position 53 to 59 of the G-CSF with 177 amino acids, or/and at least one of the four histidine residues at positions 43, 79, 156 and 170 of the mature G-CSF with 174 amino acids or at positions 46, 82, 159, or 173 of the mature G-CSF with 177 amino acids.

GB 2 213 821, entitled "Synthetic Human Granulocyte Colony Stimulating Factor Gene" reportedly discloses a synthetic G-CSF-encoding nucleic acid sequence incorporating restriction sites to facilitate the cassette mutagenesis of selected regions, and flanking restriction sites to facilitate the incorporation of the gene into a desired expression system.

G-CSF has reportedly been crystallized to some extent, e.g., EP 344 796, and the overall structure of G-CSF has been surmised, but only on a gross level. Bazan, Immunology Today 11: 350-354 (1990); Parry et al., J. Molecular Recognition 8: 107-110 (1988). To date, there have been no reports of the overall structure of G-CSF, and no systematic studies of the relationship of the overall structure and function of the molecule, studies which are essential to the systematic design of G-CSF analogs. Accordingly, there exists a need for a method of this systematic design of G-CSF analogs, and the resultant compositions.

Summary of the Invention

The three dimensional structure of G-CSF has now been determined to the atomic level. From this three-dimensional structure, one can now forecast with substantial certainty how changes in the composition of a G-CSF molecule may result in structural changes. These structural characteristics may be correlated with biological activity to design and produce G-CSF analogs.

Although others had speculated regarding the three dimensional structure of G-CSF, Bazan, Immunology Today 11: 350-354 (1990); Parry et al., J. Molecular Recognition 8: 107-110 (1988), these speculations were of no help to those wishing to prepare G-CSF analogs either because the surmised structure was incorrect (Parry et al., *supra*) and/or because the surmised structure provided no detail correlating the constituent moieties with structure. The present determination of the three-dimensional structure to the atomic level is by far the most complete analysis to date, and provides important information to those wishing to design and prepare G-CSF analogs. For example, from the present three dimensional structural analysis, precise areas of hydrophobicity and hydrophilicity have been determined.

Relative hydrophobicity is important because it directly relates to the stability of the molecule. Generally, biological molecules, found in aqueous environments, are externally hydrophilic and internally hydrophobic; in accordance with the second law of thermodynamics provides, this is the lowest energy state and provides for stability. Although one could have speculated that G-CSF's internal core would be hydrophobic, and the outer areas would be hydrophilic, one would have had no way of knowing specific hydrophobic or hydrophilic areas. With the presently provided knowledge of areas of hydrophobic-

ity/philiicity, one may forecast with substantial certainty which changes to the G-CSF molecule will affect the overall structure of the molecule.

As a general rule, one may use knowledge of the geography of the hydrophobic and hydrophilic regions to design analogs in which the overall G-CSF structure is not changed, but change does affect biological activity ("biological activity" being used here in its broadest sense to denote function). One may correlate biological activity to structure. If the structure is not changed, and the mutation has no effect on biological activity, then the mutation has no biological function. If, however, the structure is not changed and the mutation does affect biological activity, then the residue (or atom) is essential to at least one biological function. Some of the present working examples were designed to provide no change in overall structure, yet have a change in biological function.

Based on the correlation of structure to biological activity, one aspect of the present invention relates to G-CSF analogs. These analogs are molecules which have more, fewer, different or modified amino acid residues from the G-CSF amino acid sequence. The modifications may be by addition, substitution, or deletion of one or more amino acid residues. The modification may include the addition or substitution of analogs of the amino acids themselves, such as peptidomimetics or amino acids with altered moieties such as altered side groups. The G-CSF used as a basis for comparison may be of human, animal or recombinant nucleic acid-technology origin (although the working examples disclosed herein are based on the recombinant production of the 174 amino acid species of human G-CSF, having an extra N-terminus methionyl residue). The analogs may possess functions different from natural human G-CSF molecule, or may exhibit the same functions, or varying degrees of the same functions. For example, the analogs may be designed to have a higher or lower biological activity, have a longer shelf-life or a decrease in stability, be easier to formulate, or more difficult to combine with other ingredients. The analogs may have no hematopoietic activity, and may therefore be useful as an antagonist against G-CSF effect (as, for example, in the overproduction of G-CSF). From time to time herein the present analogs are referred to as proteins or peptides for convenience, but contemplated herein are other types of molecules, such as peptidomimetics or chemically modified peptides.

In another aspect, the present invention relates to related compositions containing a G-CSF analog as an active ingredient. The term, "related composition," as used herein, is meant to denote a composition which may be obtained once the identity of the G-CSF analog is ascertained (such as a G-CSF analog labeled with a detectable label, related receptor or pharmaceutical composition). Also considered a related composition are chemically modified versions of the G-CSF analog, such as those having attached at least one polyethylene glycol molecule.

For example, one may prepare a G-CSF analog to which a detectable label is attached, such as a fluorescent, chemiluminescent or radioactive molecule.

Another example is a pharmaceutical composition which may be formulated by known techniques using known materials, *see, e.g.*, Remington's Pharmaceutical Sciences, 18th Ed. (1990, Mack Publishing Co., Easton, Pennsylvania 18042) pages 1435-1712, which are herein incorporated by reference. Generally, the formulation will depend on a variety of factors such as administration, stability, production concerns and other factors. The G-CSF analog may be administered by injection or by pulmonary administration via inhalation. Enteric dosage forms may also be available for the present G-CSF analog compositions, and therefore oral administration may be effective. G-CSF analogs may be inserted into liposomes or other microcarriers for delivery, and may be formulated in gels or other compositions for sustained release. Although preferred compositions will vary depending on the use to which the composition will be put, generally, for G-CSF analogs having at least one of the biological activities of natural G-CSF, preferred pharmaceutical compositions are those prepared for subcutaneous injection or for pulmonary administration via inhalation, although the particular formulations for each type of administration will depend on the characteristics of the analog.

Another example of related composition is a receptor for the present analog. As used herein, the term "receptor" indicates a moiety which selectively binds to the present analog molecule. For example, antibodies, or fragments thereof, or "recombinant antibodies" (*see* Huse *et al.*, *Science* 248:1275 (1989)) may be used as receptors. Selective binding does not mean only specific binding (although binding-specific receptors are encompassed herein), but rather that the binding is not a random event. Receptors may be on the cell surface or intra- or extra-cellular, and may act to effectuate, inhibit or localize the biological activity of the present analogs. Receptor binding may also be a triggering mechanism for a cascade of activity indirectly related to the analog itself. Also contemplated herein are nucleic acids, vectors containing such nucleic acids and host cells containing such nucleic acids which encode such receptor.

Another example of a related composition is a G-CSF analog with a chemical moiety attached. Generally, chemical modification may alter biological activity or antigenicity of a protein, or may alter other

characteristics, and these factors will be taken into account by a skilled practitioner. As noted above, one example of such chemical moiety is polyethylene glycol. Modification may include the addition of one or more hydrophilic or hydrophobic polymer molecules, fatty acid molecules, or polysaccharide molecules. Examples of chemical modifiers include polyethylene glycol, alkylpolyethylene glycols, Di-poly(amino acids), polyvinylpyrrolidone, polyvinyl alcohol, pyran copolymer, acetic acid/acetylation, propionic acid, palmitic acid, stearic acid, dextran, carboxymethyl cellulose, pullulan, or agarose. See, Francis, *Focus on Growth Factors* 3: 4-10 (May 1992) (published by Mediscript, Mountview Court, Friern Barnet Lane, London N20 0LD, UK). Also, chemical modification may include an additional protein or portion thereof, use of a cytotoxic agent, or an antibody. The chemical modification may also include lecithin.

In another aspect, the present invention relates to nucleic acids encoding such analogs. The nucleic acids may be DNAs or RNAs or derivatives thereof, and will typically be cloned and expressed on a vector, such as a phage or plasmid containing appropriate regulatory sequences. The nucleic acids may be labeled (such as using a radioactive, chemiluminescent, or fluorescent label) for diagnostic or prognostic purposes, for example. The nucleic acid sequence may be optimized for expression, such as including codons preferred for bacterial expression. The nucleic acid and its complementary strand, and modifications thereof which do not prevent encodement of the desired analog are here contemplated.

In another aspect, the present invention relates to host cells containing the above nucleic acids encoding the present analogs. Host cells may be eukaryotic or prokaryotic, and expression systems may include extra steps relating to the attachment (or prevention) of sugar groups (glycosylation), proper folding of the molecule, the addition or deletion of leader sequences or other factors incident to recombinant expression.

In another aspect the present invention relates to antisense nucleic acids which act to prevent or modify the type or amount of expression of such nucleic acid sequences. These may be prepared by known methods.

In another aspect of the present invention, the nucleic acids encoding a present analog may be used for gene therapy purposes, for example, by placing a vector containing the analog-encoding sequence into a recipient so the nucleic acid itself is expressed inside the recipient who is in need of the analog composition. The vector may first be placed in a carrier, such as a cell, and then the carrier placed into the recipient. Such expression may be localized or systemic. Other carriers include non-naturally occurring carriers, such as liposomes or other microcarriers or particles, which may act to mediate gene transfer into a recipient.

The present invention also provides for computer programs for the expression (such as visual display) of the G-CSF or analog three dimensional structure, and further, a computer program which expresses the identity of each constituent of a G-CSF molecule and the precise location within the overall structure of that constituent, down to the atomic level. Set forth below is one example of such program. There are many currently available computer programs for the expression of the three dimensional structure of a molecule. Generally, these programs provide for inputting of the coordinates for the three dimensional structure of a molecule (i.e., for example, a numerical assignment for each atom of a G-CSF molecule along an x, y, and z axis), means to express (such as visually display) such coordinates, means to alter such coordinates and means to express an image of a molecule having such altered coordinates. One may program crystallographic information, i.e., the coordinates of the location of the atoms of a G-CSF molecule in three dimension space, wherein such coordinates have been obtained from crystallographic analysis of said G-CSF molecule, into such programs to generate a computer program for the expression (such as visual display) of the G-CSF three dimensional structure. Also provided, therefore, is a computer program for the expression of G-CSF analog three dimensional structure. Preferred is the computer program Insight II, version 4, available from Biosym, San Diego, California, with the coordinates as set forth in FIGURE 5 input. Preferred expression means is on a Silicon Graphics 320 VGX computer, with Crystal Eyes glasses (also available from Silicon Graphics), which allows one to view the G-CSF molecule or its analog stereoscopically. Alternatively, the present G-CSF crystallographic coordinates and diffraction data are also deposited in the Protein Data Bank, Chemistry Department, Brookhaven National Laboratory, Upton, New York 119723, USA. One may use these data in preparing a different computer program for expression of the three dimensional structure of a G-CSF molecule or analog thereof. Therefore, another aspect of the present invention is a computer program for the expression of the three dimensional structure of a G-CSF molecule. Also provided is said computer program for visual display of the three dimensional structure of a G-CSF molecule; and further, said program having means for altering such visual display. Apparatus useful for expression of such computer program, particularly for the visual display of the computer image of said three dimensional structure of a G-CSF molecule or analog thereof is also therefore here provided, as well as means for preparing said computer program and apparatus.

The computer program is useful for preparation of G-CSF analogs because one may select specific sites on the G-CSF molecule for alteration and readily ascertain the effect the alteration will have on the overall structure of the G-CSF molecule. Selection of said site for alteration will depend on the desired biological characteristic of the G-CSF analog. If one were to randomly change said G-CSF molecule (r-met-hu-G-CSF) there would be 175^{20} possible substitutions, and even more analogs having multiple changes, additions or deletions. By viewing the three dimensional structure wherein said structure is correlated with the composition of the molecule, the selection for sites of alteration is no longer a random event, but sites for alteration may be determined rationally.

As set forth above, identity of the three dimensional structure of G-CSF, including the placement of each constituent down to the atomic level has now yielded information regarding which moieties are necessary to maintain the overall structure of the G-CSF molecule. One may therefore select whether to maintain the overall structure of the G-CSF molecule when preparing a G-CSF analog of the present invention, or whether (and how) to change the overall structure of the G-CSF molecule when preparing a G-CSF analog of the present invention. Optionally, once one has prepared such analog, one may test such analog for a desired characteristic.

One may, for example, seek to maintain the overall structure possessed by a non-altered natural or recombinant G-CSF molecule. The overall structure is presented in Figures 2, 3, and 4, and is described in more detail below. Maintenance of the overall structure may ensure receptor binding, a necessary characteristic for an analog possessing the hematopoietic capabilities of natural G-CSF (if no receptor binding, signal transduction does not result from the presence of the analog). It is contemplated that one class of G-CSF analogs will possess the three dimensional core structure of a natural or recombinant (non-altered) G-CSF molecule, yet possess different characteristics, such as an increased ability to selectively stimulate neutrophils. Another class of G-CSF analogs are those with a different overall structure which diminishes the ability of a G-CSF analog molecule to bind to a G-CSF receptor, and possesses a diminished ability to selectively stimulate neutrophils as compared to non-altered natural or recombinant G-CSF.

For example, it is now known which moieties within the internal regions of the G-CSF molecule are hydrophobic, and, correspondingly, which moieties on the external portion of the G-CSF molecule are hydrophilic. Without knowledge of the overall three dimensional structure, preferably to the atomic level as provided herein, one could not forecast which alterations within this hydrophobic internal area would result in a change in the overall structural conformation of the molecule. An overall structural change could result in a functional change, such as lack of receptor binding, for example, and therefore, diminishment of biological activity as found in non-altered G-CSF. Another class of G-CSF analogs is therefore G-CSF analogs which possess the same hydrophobicity as (non-altered) natural or recombinant G-CSF. More particularly, another class of G-CSF analogs possesses the same hydrophobic moieties within the four helical bundle of its internal core as those hydrophobic moieties possessed by (non-altered) natural or recombinant G-CSF yet have a composition different from said non-altered natural or recombinant G-CSF.

Another example relates to external loops which are structures which connect the internal core (helices) of the G-CSF molecule. From the three dimensional structure -- including information regarding the spatial location of the amino acid residues -- one may forecast that certain changes in certain loops will not result in overall conformational changes. Therefore, another class of G-CSF analogs provided herein is that having an altered external loop but possessing the same overall structure as (non-altered) natural or recombinant G-CSF. More particularly, another class of G-CSF analogs provided herein are those having an altered external loop, said loop being selected from the loop present between helices A and B; between helices B and C; between helices C and D; between helices D and A, as those loops and helices are identified herein. More particularly, said loops, preferably the AB loop and/or the CD loop are altered to increase the half life of the molecule by stabilizing said loops. Such stabilization may be by connecting all or a portion of said loop(s) to a portion of an alpha helical bundle found in the core of a G-CSF (or analog) molecule. Such connection may be via beta sheet, salt bridge, disulfide bonds, hydrophobic interaction or other connecting means available to those skilled in the art, wherein such connecting means serves to stabilize said external loop or loops. For example, one may stabilize the AB or CD loops by connecting the AB loop to one of the helices within the internal region of the molecule.

The N-terminus also may be altered without change in the overall structure of a G-CSF molecule, because the N-terminus does not effect structural stability of the internal helices, and, although the external loops are preferred for modification, the same general statements apply to the N-terminus.

Additionally, such external loops may be the site(s) for chemical modification because in (non-altered) natural or recombinant G-CSF such loops are relatively flexible and tend not to interfere with receptor binding. Thus, there would be additional room for a chemical moiety to be directly attached (or indirectly

attached via another chemical moiety which serves as a chemical connecting means). The chemical moiety may be selected from a variety of moieties available for modification of one or more function of a G-CSF molecule. For example, an external loop may provide sites for the addition of one or more polymer which serves to increase serum half-life, such as a polyethylene glycol molecule. Such polyethylene glycol molecule(s) may be added wherein said loop is altered to include additional lysines which have reactive side groups to which polyethylene glycol moieties are capable of attaching. Other classes of chemical moieties may also be attached to one or more external loops, including but not limited to other biologically active molecules, such as receptors, other therapeutic proteins (such as other hematopoietic factors which would engender a hybrid molecule), or cytotoxic agents (such as diphtheria toxin). This list is of course not complete; one skilled in the art possessed of the desired chemical moiety will have the means to effect attachment of said desired moiety to the desired external loop. Therefore, another class of the present G-CSF analogs includes those with at least one alteration in an external loop wherein said alteration provides for the addition of a chemical moiety such as at least one polyethylene glycol molecule.

Deletions, such as deletions of sites recognized by proteins for degradation of the molecule, may also be effectual in the external loops. This provides alternative means for increasing half-life of a molecule otherwise having the G-CSF receptor binding and signal transduction capabilities (i.e., the ability to selectively stimulate the maturation of neutrophils). Therefore, another class of the present G-CSF analogs includes those with at least one alteration in an external loop wherein said alteration decreases the turnover of said analog by proteases. Preferred loops for such alterations are the AB loop and the CD loop. One may prepare an abbreviated G-CSF molecule by deleting a portion of the amino acid residues found in the external loops (identified in more detail below), said abbreviated G-CSF molecule may have additional advantages in preparation or in biological function.

Another example relates to the relative charges between amino acid residues which are in proximity to each other. As noted above, the G-CSF molecule contains a relatively tightly packed four helical bundle. Some of the faces on the helices face other helices. At the point (such as a residue) where a helix faces another helix, the two amino acid moieties which face each other may have the same charge, and thus tend to repel each other, which lends instability to the overall molecule. This may be eliminated by changing the charge (to an opposite charge or a neutral charge) of one or both of the amino acid moieties so that there is no repelling. Therefore, another class of G-CSF analogs includes those G-CSF analogs having been altered to modify instability due to surface interactions, such as electron charge location.

In another aspect, the present invention relates to methods for designing G-CSF analogs and related compositions and the products of those methods. The end products of the methods may be the G-CSF analogs as defined above or related compositions. For instance, the examples disclosed herein demonstrate (a) the effects of changes in the constituents (i.e., chemical moieties) of the G-CSF molecule on the G-CSF structure and (b) the effects of changes in structure on biological function. Essentially, therefore, another aspect of the present invention is a method for preparing a G-CSF analog comprising the steps of:

- (a) viewing information conveying the three dimensional structure of a G-CSF molecule wherein the chemical moieties, such as each amino acid residue or each atom of each amino acid residue, of the G-CSF molecule are correlated with said structure;
- (b) selecting from said information a site on a G-CSF molecule for alteration;
- (c) preparing a G-CSF analog molecule having such alteration; and
- (d) optionally, testing such G-CSF analog molecule for a desired characteristic.

One may use the here provided computer programs for a computer-based method for preparing a G-CSF analog. Another aspect of the present invention is therefore a computer based method for preparing a G-CSF analog comprising the steps of:

- (a) providing computer expression of the three dimensional structure of a G-CSF molecule wherein the chemical moieties, such as each amino acid residue or each atom of each amino acid residue, of the G-CSF molecule are correlated with said structure;
- (b) selecting from said computer expression a site on a G-CSF molecule for alteration;
- (c) preparing a G-CSF molecule having such alteration; and
- (d) optionally, testing such G-CSF molecule for a desired characteristic.

More specifically, the present invention provides a method for preparing a G-CSF analog comprising the steps of:

- (a) viewing the three dimensional structure of a G-CSF molecule via a computer, said computer programmed (i) to express the coordinates of a G-CSF molecule in three dimensional space, and (ii) to allow for entry of information for alteration of said G-CSF expression and viewing thereof;
- (b) selecting a site on said visual image of said G-CSF molecule for alteration;
- (c) entering information for said alteration on said computer;

- (d) viewing a three dimensional structure of said altered G-CSF molecule via said computer;
- (e) optionally repeating steps (a)-(e);
- (f) preparing a G-CSF analog with said alteration; and
- (g) optionally testing said G-CSF analog for a desired characteristic.

5 In another aspect, the present invention relates to methods of using the present G-CSF analogs and related compositions and methods for the treatment or protection of mammals, either alone or in combination with other hematopoietic factors or drugs in the treatment of hematopoietic disorders. It is contemplated that one aspect of designing G-CSF analogs will be the goal of enhancing or modifying the characteristics non-modified G-CSF is known to have.

10 For example, the present analogs may possess enhanced or modified activities, so, where G-CSF is useful in the treatment of (for example) neutropenia, the present compositions and methods may also be of such use.

Another example is the modification of G-CSF for the purpose of interacting more effectively when used in combination with other factors particularly in the treatment of hematopoietic disorders. One example of such combination use is to use an early-acting hematopoietic factor (i.e., a factor which acts earlier in the hematopoiesis cascade on relatively undifferentiated cells) and either simultaneously or in serial use of a later-acting hematopoietic factor, such as G-CSF or analog thereof (as G-CSF acts on the CFU-GM lineage in the selective stimulation of neutrophils). The present methods and compositions may be useful in therapy involving such combinations or "cocktails" of hematopoietic factors.

20 The present compositions and methods may also be useful in the treatment of leukopenia, myelogenous leukemia, severe chronic neutropenia, aplastic anemia, glycogen storage disease, mucositis, and other bone marrow failure states. The present compositions and methods may also be useful in the treatment of hematopoietic deficits arising from chemotherapy or from radiation therapy. The success of bone marrow transplantation, or the use of peripheral blood progenitor cells for transplantation, for example, may be enhanced by application of the present compositions (proteins or nucleic acids for gene therapy) and methods. The present compositions and methods may also be useful in the treatment of infectious diseases, such in the context of wound healing, burn treatment, bacteremia, septicemia, fungal infections, endocarditis, osteomyelitis, infection related to abdominal trauma, infections not responding to antibiotics, pneumonia and the treatment of bacterial inflammation may also benefit from the application of the present compositions and methods. In addition, the present compositions and methods may be useful in the treatment of leukemia based upon a reported ability to differentiate leukemic cells. Welte et al., *PNAS-USA* 82: 1526-1530 (1985). Other applications include the treatment of individuals with tumors, using the present compositions and methods, optionally in the presence of receptors (such as antibodies) which bind to the tumor cells. For review articles on therapeutic applications, see Lieshke and Burgess, *N.Engl.J.Med.* 327: 28-34 and 99-106 (1992) both of which are herein incorporated by reference.

30 The present compositions and methods may also be useful to act as intermediaries in the production of other moieties; for example, G-CSF has been reported to influence the production of other hematopoietic factors and this function (if ascertained) may be enhanced or modified via the present compositions and/or methods.

40 The compositions related to the present G-CSF analogs, such as receptors, may be useful to act as an antagonist which prevents the activity of G-CSF or an analog. One may obtain a composition with some or all of the activity of non-altered G-CSF or a G-CSF analog, and add one or more chemical moieties to alter one or more properties of such G-CSF or analog. With knowledge of the three dimensional conformation, one may forecast the best geographic location for such chemical modification to achieve the desired effect.

45 General objectives in chemical modification may include improved half-life (such as reduced renal, immunological or cellular clearance), altered bioactivity (such as altered enzymatic properties, dissociated bioactivities or activity in organic solvents), reduced toxicity (such as concealing toxic epitopes, compartmentalization, and selective biodistribution), altered immunoreactivity (reduced immunogenicity, reduced antigenicity or adjuvant action), or altered physical properties (such as increased solubility, improved thermal stability, improved mechanical stability, or conformational stabilization). See Francis, *Focus on Growth Factors* 3: 4-10 (May 1992) (published by Mediscript, Mountview Court, Friern Barnet Lane, London N20 0LD, UK).

50 The examples below are illustrative of the present invention and are not intended as a limitation. It is understood that variations and modifications will occur to those skilled in the art, and it is intended that the appended claims cover all such equivalent variations which come within the scope of the invention as claimed.

Detailed Description of the Drawings

FIGURE 1 is an illustration of the amino acid sequence of the 174 amino acid species of G-CSF with an additional N-terminal methionine (Seq. ID No.: 1) (Seq. ID No.: 2).

FIGURE 2 is a topology diagram of the crystalline structure of G-CSF, as well as hGH, pGH, GM-CSF, INF-B, IL-2, and IL-4. These illustrations are based on inspection of cited references. The length of secondary structural elements are drawn in proportion to the number of residues. A, B, C, and D helices are labeled according to the scheme used herein for G-CSF. For INF- β , the original labeling of helices is indicated in parentheses.

FIGURE 3 is a "ribbon diagram" of the three dimensional structure of G-CSF. Helix A is amino acid residues 11-39 (numbered according to Figure 1, above), helix B is amino acid residues 72-91, helix C is amino acid residues 100-123, and helix D is amino acid residues 143-173. The relatively short 3^{10} helix is at amino acid residues 45-48, and the alpha helix is at amino acid residues 48-53. Residues 93-95 form almost one turn of a left handed helix.

FIGURE 4 is a "barrel diagram" of the three dimensional structure of G-CSF. Shown in various shades of gray are the overall cylinders and their orientations for the three dimensional structure of G-CSF. The numbers indicate amino acid residue position according to FIGURE 1 above.

FIGURE 5 is a list of the coordinates used to generate a computer-aided visual image of the three-dimensional structure of G-CSF. The coordinates are set forth below. The columns correspond to separate field:

- (i) Field 1 (from the left hand side) is the atom,
- (ii) Field 2 is the assigned atom number,
- (iii) Field 3 is the atom name (according to the periodic table standard nomenclature, with CB being carbon atom Beta, CG is Carbon atom Gamma, etc.);
- (iv) Field 4 is the residue type (according to three letter nomenclature for amino acids as found in, e.g., Stryer, Biochemistry, 3d Ed., W.H. Freeman and Company, N.Y. 1988, inside back cover);
- (v) Fields 5-7 are the x-axis, y-axis and z-axis positions of the atom;
- (vi) Field 8 (often a "1.00") designates occupancy at that position;
- (vii) Field 9 designates the B-factor;
- (viii) Field 10 designates the molecule designation. Three molecules (designated a, b, and c) of G-CSF crystallized together as a unit. The designation a, b, or c indicates which coordinates are from which molecule. The number after the letter (1, 2, or 3) indicates the assigned amino acid residue position, with molecule A having assigned positions 10-175, molecule B having assigned positions 210-375, and molecule C having assigned positions 410-575. These positions were so designated so that there would be no overlap among the three molecules which crystallized together. (The "W" designation indicates water).

FIGURE 6 is a schematic representation of the strategy involved in refining the crystallization matrix for parameters involved in crystallization. The crystallization matrix corresponds to the final concentration of the components (salts, buffers and precipitants) of the crystallization solutions in the wells of a 24 well tissue culture plate. These concentrations are produced by pipetting the appropriate volume of stock solutions into the wells of the microtiter plate. To design the matrix, the crystallographer decides on an upper and lower concentration of the component. These upper and lower concentrations can be pipetted along either the rows (e.g., A1-A6, B1-B6, C1-C6 or D1-D6) or along the entire tray (A1-D6). The former method is useful for checking reproducibility of crystal growth of a single component along a limited number of wells, whereas the latter method is more useful in initial screening. The results of several stages of refinement of the crystallization matrix are illustrated by a representation of three plates. The increase in shading in the wells indicates a positive crystallization result which, in the final stages, would be X-ray quality crystals but in the initial stages could be oil droplets, granular precipitates or small crystals approximately less than 0.05 mm in size. Part A represents an initial screen of one parameter in which the range of concentration between the first well (A1) and last well (D6) is large and the concentration increase between wells is calculated as $(\text{concentration A1} - (\text{concentration D6})) / 23$. Part B represents that in later stages of the crystallization matrix refinement of the concentration spread between A1 and D6 would be reduced which would result in more crystals formed per plate. Part C indicates a final stage of matrix refinement in which quality crystals are found in most wells of the plate.

Detailed Description of the invention

The present invention grows out of the discovery of the three dimensional structure of G-CSF. This three dimensional structure has been expressed via computer program for stereoscopic viewing. By viewing this stereoscopically, structure-function relationships identified and G-CSF analogs have been designed and made.

The Overall Three Dimensional Structure of G-CSF

The G-CSF used to ascertain the structure was a non-glycosylated 174 amino acid species having an extra N-terminal methionine residue incident to bacterial expression. The DNA and amino acid sequence of this G-CSF are illustrated in FIGURE 1.

Overall, the three dimensional structure of G-CSF is predominantly helical, with 103 of the 175 residues forming a 4-alpha-helical bundle. The only other secondary structure is found in the loop between the first two long helices where a 4 residue 3^{10} helix is immediately followed by a 6 residue alpha helix. As shown in FIGURE 2, the overall structure has been compared with the structure reported for other proteins: growth hormone (Abdel-Meguid et al., PNAS-USA 84: 6434 (1987) and Vos et al., Science 255: 305-312 (1992)), granulocyte macrophage colony stimulating factor (Diederichs et al., Science 254: 1779-1782 (1991)), interferon- β (Senda et al., EMBO J. 11: 3193-3201 (1992)), interleukin-2 (McKay Science 257: 1673-1677 (1992)) and interleukin-4 (Powers et al., Science 256: 1673-1677 (1992), and Smith et al., J. Mol. Biol. 224: 899-904 (1992)). Structural similarity among these growth factors occurs despite the absence of similarity in their amino acid sequences.

Presently, the structural information was correlation of G-CSF biochemistry, and this can be summarized as follows (with sequence position 1 being at the N-terminus):

Sequence Position	Description of Structure	Analysis
1-10	Extended chain	Deletion causes no loss of biological activity
Cys 18	Partially buried	Reactive with DTNB and Thimerosol but not with iodo-acetate
34	Alternative splice site	Insertion reduces biological activity
20-47 (inclusive)	Helix A, first disulfide and portion of AB helix	Predicted receptor binding region based on neutralizing antibody data
20, 23, 24	Helix A	Single alanine mutation of residue(s) reduces biological activity. Predicted receptor binding (Site B).
165-175 (inclusive)	Carboxy terminus	Deletion reduces biological activity

This biochemical information, having been gleaned from antibody binding studies, see Layton et al., Biochemistry 26: 23815-23823 (1991), was superimposed on the three-dimensional structure in order to design G-CSF analogs. The design, preparation, and testing of these G-CSF analogs is described in Example 1 below.

EXAMPLE 1

This Example describes the preparation of crystalline G-CSF, the visualization of the three dimensional structure of recombinant human G-CSF via computer-generated image, the preparation of analogs, using site-directed mutagenesis or nucleic acid amplification methods, the biological assays and HPLC analysis used to analyze the G-CSF analogs, and the resulting determination of overall structure/function relationships. All cited publications are herein incorporated by reference.

A. Use of Automated Crystallization

The need for a three-dimensional structure of recombinant human granulocyte colony stimulating factor (r-hu-G-CSF), and the availability of large quantities of the purified protein, led to methods of crystal growth by incomplete factorial sampling and seeding. Starting with the implementation of incomplete factorial

crystallization described by Jancarik and Kim: J. Appl. Crystallogr. 24: 409 (1991) solution conditions that yielded oil droplets and birefringence aggregates were ascertained. Also, software and hardware of an automated pipetting system were modified to produce some 400 different crystallization conditions per day. Weber, J. Appl. Crystallogr. 20: 366-373 (1987). This procedure led to a crystallization solution which produced r-hu-G-CSF crystals.

The size, reproducibility and quality of the crystals was improved by a seeding method in which the number of "nucleation initiating units" was estimated by serial dilution of a seeding solution. These methods yielded reproducible growth of 2.0 mm r-hu-G-CSF crystals. The space group of these crystals is P2₁2₁2₁, with cell dimensions of a = 90 Å, b = 110 Å and c = 49 Å, and they diffract to a resolution of 2.0 Å.

1. Overall Methodology

To search for the crystallizing conditions of a new protein, Carter and Carter, J. Biol. Chem. 254: 122219-12223 (1979) proposed the incomplete factorial method. They suggested that a sampling of a large number of randomly selected, but generally probable, crystallizing conditions may lead to a successful combination of reagents that produce protein crystallization. This idea was implemented by Jancarik and Kim, J. Appl. Crystallogr. 24: 409(1991), who described 32 solutions for the initial crystallization trials which cover a range of pH, salts and precipitants. Here we describe an extension of their implementation to an expanded set of 70 solutions. To minimize the human effort and error of solution preparation, the method has been programmed for an automatic pipetting machine.

Following Weber's method of successive automated grid searching (SAGS), J.Cryst. Growth 90: 318-324(1988), the robotic system was used to generate a series of solutions which continually refined the crystallization conditions of temperature, pH, salts and precipitant. Once a solution that could reproducibly grow crystals was determined, a seeding technique which greatly improved the quality of the crystals was developed. When these methods were combined, hundreds of diffraction quality crystals (crystals diffracting to at least about 2.5 Angstroms, preferably having at least portions diffracting to below 2 Angstroms, and more preferably, approximately 1 Angstrom) were produced in a few days.

Generally, the method for crystallization, which may be used with any protein one desires to crystallize, comprises the steps of:

- (a) combining aqueous aliquots of the desired protein with either (i) aliquots of a salt solution, each aliquot having a different concentration of salt; or (ii) aliquots of a precipitant solution, each aliquot having a different concentration of precipitant, optionally wherein each combined aliquot is combined in the presence of a range of pH;
- (b) observing said combined aliquots for precrystalline formations, and selecting said salt or precipitant combination and said pH which is efficacious in producing precrystalline forms, or, if no precrystalline forms are so produced, increasing the protein starting concentration of said aqueous aliquots of protein;
- (c) after said salt or said precipitant concentration is selected, repeating step (a) with said previously unselected solution in the presence of said selected concentration; and
- (d) repeating step (b) and step (a) until a crystal of desired quality is obtained.

The above method may optionally be automated, which provides vast savings in time and labor. Preferred protein starting concentrations are between 10mg/ml and 20mg/ml, however this starting concentration will vary with the protein (the G-CSF below was analyzed using 33mg/ml). A preferred range of salt solution to begin analysis with is (NaCl) of 0-2.5M. A preferred precipitant is polyethylene glycol 8000, however, other precipitants include organic solvents (such as ethanol), polyethylene glycol molecules having a molecular weight in the range of 500-20,000, and other precipitants known to those skilled in the art. The preferred pH range is pH 4.5, 5.0, 5.5, 6.0, 6.5, 7.0, 7.5, 8.0, 8.5, and 9.0. Precrystallization forms include oils, birefringement precipitants, small crystals (< approximately 0.05 mm), medium crystals (approximately 0.5 to 5 mm) and large crystals (> approximately 0.5 mm). The preferred time for waiting to see a crystalline structure is 48 hours, although weekly observation is also preferred, and generally, after about one month, a different protein concentration is utilized (generally the protein concentration is increased). Automation is preferred, using the Acculux system as modified. The preferred automation parameters are described below.

Generally, protein with a concentration between 10 mg/ml and 20 mg/ml was combined with a range of NaCl solutions from 0-2.5 M, and each such combination was performed (separately) in the presence of the above range of concentrations. Once a precrystallization structure is observed, that salt concentration and pH range are optimized in a separate experiment, until the desired crystal quality is achieved. Next, the precipitant concentration, in the presence of varying levels of pH is also optimized. When both are optimized, the optimal conditions are performed at once to achieve the desired result (this is diagrammed in

FIGURE 6).

a. Implementation of an automated pipetting system

5 Drops and reservoir solutions were prepared by an Accuflex pipetting system (ICN Pharmaceuticals, Costa Mesa, CA) which is controlled by a personal computer that sends ASCII codes through a standard serial interface. The pipetter samples six different solutions by means of a rotating valve and pipettes these solutions onto a plate whose translation in a x-y coordinate system can be controlled. The vertical component of the system manipulates a syringe that is capable both of dispensing and retrieving liquid.

10 The software provided with the Accuflex was based on the SAGS method as proposed by Cox and Weber, J.Appl. Crystallogr. 20: 366-373 (1987). This method involves the systematic variation of two major crystallization parameters, pH and precipitant concentration, with provision to vary two others. While building on these concepts, the software used here provided greater flexibility in the design and implementation of the crystallization solutions used in the automated grid searching strategy. As a result of this flexibility the present software also created a larger number of different solutions. This is essential for the implementation of the incomplete factorial method as described in that section below.

To improve the speed and design of the automated grid searching strategy, the Accuflex pipetting system required software and hardware modifications. The hardware changes allowed the use of two different micro-liter trays, one used for handling drop and one used for sitting drop experiments, and a Plexiglas tray which held 24 additional buffer, salt and precipitant solutions. These additional solutions expanded the grid of crystallizing conditions that could be surveyed.

To utilize the hardware modifications, the pipetting software was written in two subroutines; one subroutine allows the crystallographer to design a matrix of crystallization solutions based on the concentrations of their components and the second subroutine to translate these concentrations into the computer code which pipettes the proper volumes of the solutions into the crystallization trays. The concentration matrices can be generated by either of two programs. The first program (MRF, available from Amgen, Inc., Thousand Oaks, CA) refers to a list of stock solution concentrations supplied by the crystallographer and calculates the required volume to be pipette to achieve the designated concentration. The second method, which is preferred, incorporates a spread sheet program (Lotus) which can be used to make more sophisticated gradients of precipitants or pH. The concentration matrix created by either program is interpreted by the control program (SUX, a modification of the program found in the Accuflex pipetter originally and available from Amgen, Inc., Thousand Oaks, CA) and the wells are filled accordingly.

b. Implementation of the Incomplete Factorial Method

35 The convenience of the modified pipetting system for preparing diverse solutions improved the implementation of an expanded incomplete factorial method. The development of a new set of crystallization solutions having "random" components was generated using the program INFAC, Carter et al., J.Cryst. Growth 90: 60-73(1988) which produced a list containing 96 random combinations of one factor from three variables. Combinations of calcium and phosphate which immediately precipitated were eliminated, leaving 70 distinct combinations of precipitants, salts and buffers. These combinations were prepared using the automated pipetter and incubated for 1 week. The mixtures were inspected and solutions which formed precipitants were prepared again with lower concentrations of their components. This was repeated until all wells were clear of precipitant.

c. Crystallization of r-hu-G-CSF

Several different crystallization strategies were used to find a solution which produced x-ray quality crystals. These strategies included the use of the incomplete factorial method, refinement of the crystallization conditions using successive automated grid searches (SAGS), implementation of a seeding technique and development of a crystal production procedure which yielded hundreds of quality crystals overnight. Unless otherwise noted the screening and production of r-hu-G-CSF crystals utilized the hanging drop vapor diffusion method. Afinsen et al., Physical principles of protein crystallization. In: Eisenberg (ed.), Advances in Protein Chemistry 41: 1-33 (1991).

55 The initial screening for crystallization conditions of r-hu-G-CSF used the Jancarik and Kim, J.Appl.Crystallogr. 24: 409(1991) incomplete factorial method which resulted in several solutions that produced "precipitization" results. These results included birefringent precipitants, oils and very small crystals (< .05 mm). These precrystallizations solutions then served as the starting points for systematic

screening.

The screening process required the development of crystallization matrices. These matrices corresponded to the concentration of the components in the crystallization solutions and were created using the IBM-PC based spread sheet Lotus™ and implemented with the modified Accuflex pipetting system. The strategy in designing the matrices was to vary one crystallization condition (such as salt concentration) while holding the other conditions such as pH, and precipitant concentration constant. At the start of screening, the concentration range of the varied condition was large but the concentration was successively refined until all wells in the micro-titer tray produced the same crystallization result. These results were scored as follows: crystals, birefringent precipitate, granular precipitate, oil droplets and amorphous mass. If the concentration of a crystallization parameter did not produce at least a precipitant, the concentration of that parameter was increased until a precipitant formed. After each tray was produced, it was left undisturbed for at least two days and then inspected for crystal growth. After this initial screening, the trays were then inspected on a weekly basis.

From this screening process, two independent solutions with the same pH and precipitant but differing in salts (MgCl, LiSO₄) were identified which produced small (0.1 x 0.05 x 0.05 mm) crystals. Based on these results, a new series of concentration matrices were produced which varied MgCl with respect to LiSO₄ while keeping the other crystallization parameters constant. This series of experiments resulted in identification of a solution which produced diffraction quality crystals (> approximately 0.5 mm) in about three weeks. To find this crystallization growth solution (100 mM Mes pH 5.8, 380 mM MgCl₂, 220 mM LiSO₄ and 8% PEG 8k) approximately 8,000 conditions had been screened which consumed about 300 mg of protein.

The size of the crystals depended on the number of crystals forming per drop. Typically 3 to 5 crystals would be formed with average size of (1.0 x 0.7 x 0.7 mm). Two morphologies which had an identical space group (P2₁2₁2₁) and unit cell dimensions a=90.2, b=110.2, c=49.5 were obtained depending on whether or not seeding (see below) was implemented. Without seeding, the r-hu-G-CSF crystals had one long flat surface and rounded edges.

When seeding was employed, crystals with sharp faces were observed in the drop within 4 to 6 hours (0.05 by 0.05 by 0.05 mm). Within 24 hours, crystals had grown to (0.7 by 0.7 by 0.7 mm) and continued to grow beyond 2 mm depending on the number of crystals forming in the drop.

d. Seeding and determination of nucleation initiation sites.

The presently provided method for seeding crystals establishes the number of nucleation initiation units in each individual well used (here, after the optimum conditions for growing crystals had been determined). The method here is advantageous in that the number of "seeds" affects the quality of the crystals, and this in turn affects the degree of resolution. The present seeding here also provides advantages in that with seeding, G-CSF crystal grows in a period of about 3 days, whereas without seeding, the growth takes approximately three weeks.

In one series of production growth (see methods), showers of small but well defined crystals were produced overnight (<0.01 x 0.01 x 0.01 mm). Crystallization conditions were followed as described above except that a pipette tip employed in previously had been reused. Presumably, the crystal showering effect was caused by small nucleation units which had formed in the used tip and which provided sites of nucleation for the crystals. Addition of a small amount (0.5 ul) of the drops containing the crystal showers to a new drop under standard production growth conditions resulted in a shower of crystals overnight. This method was used to produce several trays of drops containing crystal showers which we termed "seed stock".

The number of nucleation initiation units (NIU) contained within the "seed stock" drops was estimated to attempt to improve the reproducibility and quality of the r-hu-G-CSF crystals. To determine the number of NIU in the "seed stock", an aliquot of the drop was serially diluted along a 96 well microtiter plate. The microtiter plate was prepared by adding 50 ul of a solution containing equal volumes of r-hu-G-CSF (33 mg/ml) and the crystal growth solution (described above) in each well. An aliquot (3 ul) of one of the "seed stock" drops was transferred to the first well of the microtiter plate. The solution in the well was mixed and 3 ul was then transferred to the next well along the row of the microtiter plate. Each row of the microtiter plate was similarly prepared and the tray was sealed with plastic tape. Overnight, small crystals formed in the bottom of the wells of the microtiter plate and the number of crystals in the wells were correlated to the dilution of the original "seed stock". To produce large single crystals, the "seed stock" drop was appropriately diluted into fresh CGS and then an aliquot of this solution containing the NIU was transferred to a drop.

Once crystallization conditions had been optimized, crystals were grown in a production method in which 3 ml each of CGS and r-hu-G-CSF (33 mg/ml) were mixed to create 5 trays (each having 24 wells). This method included the production of the refined crystallization solution in liter quantities, mixing this solution with protein and placing the protein/crystallization solution in either hanging drop or sitting drop trays. This process typically yielded 100 to 300 quality crystals (>0.5 mm) in about 5 days.

e. Experimental Methods

Materials

Crystallographic information was obtained starting with r-hu-mot-G-CSF with the amino acid sequence as provided in FIGURE 1 with a specific activity of $1.0 \pm 0.6 \times 10^6$ U/mg (as measured by cell mitogenesis assay in a 10 mM acetate buffer at pH 4.0 (in Water for Injection) at a concentration of approximately 3 mg/ml solution was concentrated with an Amicon concentrator at 75 psi using a YM10 filter. The solution was typically concentrated 10 fold at 4 °C and stored for several months.

Initial Screening

Crystals suitable for X-ray analysis were obtained by vapor-diffusion equilibrium using hanging drops. For preliminary screening, 7 μ l of the protein solution at 33 mg/ml (as prepared above) was mixed with an equal volume of the well solution, placed on siliconized glass plates and suspended over the well solution utilizing Linbro tissue culture plates (Flow Laboratories, McLean, Va). All of the pipetting was performed with the Accuflex pipetter, however, trays were removed from the automated pipetter after the well solutions had been created and thoroughly mixed for at least 10 minutes with a table top shaker. The Linbro trays were then returned to the pipetter which added the well and protein solutions to the siliconized cover slips. The cover slips were then inverted and sealed over 1 ml of the well solutions with silicon grease.

The components of the automated crystallization system are as follows. A PC-DOS computer system was used to design a matrix of crystallization solutions based on the concentration of their components. These matrices were produced with either MRF of the Lotus spread sheet (described above). The final product of these programs is a data file. This file contains the information required by the SUX program to pipette the appropriate volume of the stock solutions to obtain the concentrations described in the matrices. The SUX program information was passed through a serial I/O port and used to dictate to the Accuflex pipetting system the position of the valve relative to the stock solutions, the amount of solution to be retrieved, and then pipetted into the wells of the microtiter plates and the X-Y position of each well (the column/row of each well). Addition information was transmitted to the pipetter which included the Z position (height) of the syringe during filling as well as the position of a drain where the system pauses to purge the syringe between fillings of different solutions. The 24 well microtiter plate (either Linbro or Cryschem) and cover slip holder was placed on a plate which was moved in the X-Y plane. Movement of the plate allowed the pipetter to position the syringe to pipette into the wells. It also positioned the coverslips and vials and extract solutions from these sources. Prior the pipetting, the Linbro microtiter plates had a thin film of grease applied around the edges of the wells. After the crystallization solutions were prepared in the wells and before they were transferred to the cover slips, the microtiter plate was removed from the pipetting system, and solutions were allowed to mix on a table top shaker for ten minutes. After mixing, the well solution was either transferred to the cover slips (in the case of the hanging drop protocol) or transferred to the middle post in the well (in the case of the sitting drop protocol). Protein was extracted from a vial and added to the coverslip drop containing the well solution (or to the post). Plastic tape was applied to the top of the Cryschem plate to seal the wells.

Production Growth

Once conditions for crystallization had been optimized, crystal growth was performed utilizing a "production" method. The crystallization solution which contained 100 mM Mes pH 5.8, 380 mM MgCl₂, 220 mM LiSO₄, and 8% PEG 8K was made in 1 liter quantities. Utilizing an Eppendorf syringe pipetter, 1 ml aliquots of this solution were pipetted into each of the wells of the Linbro plate. A solution containing 50% of this solution and 50% G-CSF (33 mg/ml) was mixed and pipetted onto the siliconized cover slips. Typical volumes of these drops were between 50 and 100 μ l and because of the large size of these drops, great care was taken in flipping the coverslips and suspending the drops over the wells.

Data Collection

The structure has been refined with X-PLOR (Bruniger, X-PLOR version 3.0, A system for crystallography and NMR, Yale University, New Haven CT) against 2.2Å data collected on an R-AXIS (Molecular Structure, Corp. Houston, TX) imaging plate detector.

f. Observations

As an effective recombinant human therapeutic, r-hu-G-CSF has been produced in large quantities and gram levels have been made available for structural analysis. The crystallization methods provided herein are likely to find other applications as other proteins of interest become available. This method can be applied to any crystallographic project which has large quantities of protein (approximately >200 mg). As one skilled in the art will recognize, the present materials and methods may be modified and equivalent materials and methods may be available for crystallization of other proteins.

B. Computer Program For Visualizing The Three Dimensional Structure of G-CSF

Although diagrams, such as those in the Figures herein, are useful for visualizing the three dimensional structure of G-CSF, a computer program which allows for stereoscopic viewing of the molecule is contemplated as preferred. This stereoscopic viewing, or "virtual reality" as those in the art sometimes refer to it, allows one to visualize the structure in its three dimensional form from every angle in a wide range of resolution, from macromolecular structure down to the atomic level. The computer programs contemplated herein also allow one to change perspective of the viewing angle of the molecule, for example by rotating the molecule. The contemplated programs also respond to changes so that one may, for example, delete, add, or substitute one or more images of atoms, including entire amino acid residues, or add chemical moieties to existing or substituted groups, and visualize the change in structure.

Other computer based systems may be used; the elements being: (a) a means for entering information, such as orthogonal coordinates or other numerically assigned coordinates of the three dimensional structure of G-CSF; (b) a means for expressing such coordinates, such as visual means so that one may view the three dimensional structure and correlate such three dimensional structure with the composition of the G-CSF molecule, such as the amino acid composition; (c) optionally, means for entering information which alters the composition of the G-CSF molecule expressed, so that the image of such three dimensional structure displays the altered composition.

The coordinates for the preferred computer program used are presented in FIGURE 5. The preferred computer program is Insight II, version 4, available from Biosym in San Diego, CA. For the raw crystallographic structure, the observed intensities of the diffraction data ("F-obs") and the orthogonal coordinates are also deposited in the Protein Data Bank, Chemistry Department, Brookhaven National Laboratory, Upton, New York 119723, USA and these are herein incorporated by reference.

Once the coordinates are entered into the Insight II program, one can easily display the three dimensional G-CSF molecule representation on a computer screen. The preferred computer system for display is Silicon Graphics 320 VGX (San Diego, CA). For stereoscopic viewing, one may wear eyewear (Crystal Eyes, Silicon Graphics) which allows one to visualize the G-CSF molecule in three dimensions stereoscopically, so one may turn the molecule and envision molecular design.

Thus, the present invention provides a method of designing or preparing a G-CSF analog with the aid of a computer comprising:

- (a) providing said computer with the means for displaying the three dimensional structure of a G-CSF molecule including displaying the composition of moieties of said G-CSF molecule, preferably displaying the three dimensional location of each amino acid, and more preferably displaying the three dimensional location of each atom of a G-CSF molecule;
- (b) viewing said display;
- (c) selecting a site on said display for alteration in the composition of said molecule or the location of a moiety; and
- (d) preparing a G-CSF analog with such alteration.

The alteration may be selected based on the desired structural characteristics of the end-product G-CSF analog, and considerations for such design are described in more detail below. Such considerations include the location and compositions of hydrophobic amino acid residues, particularly residues internal to the helical structures of a G-CSF molecule which residues, when altered, alter the overall structure of the internal core of the molecule and may prevent receptor binding; the location and compositions of external

loop structures, alteration of which may not affect the overall structure of the G-CSF molecule.

FIGURES 2-4 illustrate the overall three dimensional conformation in different ways. The topological diagram, the ribbon diagram, and the barrel diagram all illustrate aspects of the conformation of G-CSF.

FIGURE 2 illustrates a comparison between G-CSF and other molecules. There is a similarity of architecture, although these growth factors differ in the local conformations of their loops and bundle geometrics. The up-up-down-down topology with two long crossover connections is conserved, however, among all six of these molecules, despite the dissimilarity in amino acid sequence.

FIGURE 3 illustrates in more detail the secondary structure of recombinant human G-CSF. This ribbon diagram illustrates the handedness of the helices and their positions relative to each other.

FIGURE 4 illustrates in a different way the conformation of recombinant human G-CSF. This "barrel" diagram illustrates the overall architecture of recombinant human G-CSF.

C. Preparation of Analogs Using M13 Mutagenesis

This example relates to the preparation of G-CSF analogs using site directed mutagenesis techniques involving the single stranded bacteriophage M13, according to methods published in PCT Application No. WO 85/00817 (Souza et al., published February 28, 1985, herein incorporated by reference). This method essentially involves using a single-stranded nucleic acid template of the non-mutagenized sequence, and binding to it a smaller oligonucleotide containing the desired change in the sequence. Hybridization conditions allow for non-identical sequences to hybridize and the remaining sequence is filled in to be identical to the original template. What results is a double stranded molecule, with one of the two strands containing the desired change. This mutagenized single strand is separated, and used itself as a template for its complementary strand. This creates a double stranded molecule with the desired change.

The original G-CSF nucleic acid sequence used is presented in FIGURE 1, and the oligonucleotides containing the mutagenized nucleic acid(s) are presented in Table 2. Abbreviations used herein for amino acid residues and nucleotides are conventional, see Stryer, Biochemistry, 3d Ed., W.H. Freeman and Company, N.Y., N.Y. 1988, inside back cover.

The original G-CSF nucleic acid sequence was first placed into vector M13mp21. The DNA from single stranded phage M13mp21 containing the original G-CSF sequence was then isolated, and resuspended in water. For each reaction, 200 ng of this DNA was mixed with a 1.5 pmole of phosphorylated oligonucleotide (Table 2) and suspended in 0.1M Tris, 0.01M MgCl₂, 0.005M DTT, 0.1mM ATP, pH 8.0. The DNAs were annealed by heating to 65°C and slowly cooling to room temperature.

Once cooled, 0.5mM of each ATP, dATP, dCTP, dGTP, TTP, 1 unit of T4 DNA ligase and 1 unit of Klenow fragment of *E. coli* polymerase 1 were added to the 1 unit of annealed DNA in 0.1M Tris, 0.025M NaCl, 0.01M MgCl₂, 0.01M DTT, pH 7.5.

The now double stranded, closed circular DNA was used to transfect *E. coli* without further purification. Plaques were screened by lifting the plaques with nitrocellulose filters, and then hybridizing the filters with single stranded DNA end-labeled with P³² for 1 hour at 55-60°C. After hybridization, the filters were washed at 0-3°C below the melt temperature of the oligo (2°C for A-T, 4°C for G-C) which selectively left autoradiography signals corresponding to plaques with phage containing the mutated sequence. Positive clones were confirmed by sequencing.

Set forth below are the oligonucleotides used for each G-CSF analog prepared via the M13 mutagenesis method. The nomenclature indicates the residue and the position of the original amino acid (e.g., Lysine at position 17), and the residue and position of the substituted amino acid (e.g., arginine 17). A substitution involving more than one residue is indicated via superscript notation, with commas between the noted positions or a semicolon indicating different residues. Deletions with no substitutions are so noted. The oligonucleotide sequences used for M13-based mutagenesis are next indicated; these oligonucleotides were manufactured synthetically, although the method of preparation is not critical, any nucleic acid synthesis method and/or equipment may be used. The length of the oligo is also indicated. As indicated above, these oligos were allowed to contact the single stranded phage vector, and then single nucleotides were added to complete the G-CSF analog nucleic acid sequence.

Table 2

G-CSE ANALOGS	SEQUENCES (5' -> 3')	Length (nucleotides)	Seq. ID
Lys17->Arg17	CTT TCT GCT GCG TTG TCT GGA ACA	24	3
Lys24->Arg24	ACA GGT TCG TCG TAT CCA GGG TG	23	4
Lys35->Arg35	CAC TGC AAG AAC GTC TGT GCG CT	23	5
Lys41->Arg41	CGC TAC TTA CCG TCT GTG CCA TC	23	6
Lys17,24,35-> Arg17,24,35	CTT TCT GCT GCG TTG TCT GGA ACA ACA GGT TCG TCG TAT CCA GGG TG CAC TGC AAG AAC GTC TGT GCG CT	24 23 23	7 8 9
Lys17,24,41-> Arg17,24,41	CTT TCT GCT GCG TTG TCT GGA ACA ACA GGT TCG TCG TAT CCA GGG TG CGC TAC TTA CCG TCT GTC CCA TC	24 23 23	10 11 12
Lys17,35,41-> Arg17,35,41	CTT TCT GCT GCG TTG TCT GGA ACA CAC TGC AAG AAC GTC TGT GCG CT CGC TAC TTA CCG TCT GTG CCA TC	24 23 23	13 14 15
Lys24,35,41-> Arg24,35,41	ACA GGT TCG TCG TAT CCA GGG TG CAC TGC AAG AAC GTC TGT GCG CT CGC TAC TTA CCG TCT GTG CCA TC	23 23 23	16 17 18

Table 2 (cont'd)

G-CSE ANALOGS	SEQUENCES (5' -> 3')	Length (nucleotides)	Seq. ID
Lys ^{17,24,35,41} -> Arg ^{17,24,35,41}	CTT TCT GCT GCG TTG TCT GGA ACA ACA GGT TCG TCG TAT CCA GGG TG CAC TGC AAG AAC GTC TGT GCG CT CGC TAC TTA CCG TCT GTG CCA TC	24 23 23 23	19 20 21 22
Cys ¹⁸ ->Ala ¹⁸ Gln ⁶⁸ ->Glu ⁶⁸ Cys ^{37,43} -> Ser ^{37,43}	TCT GCT GAA AGC TCT GGA ACA GG CTT GTC CAT CTG AAG CTC TTC AG GAA AAA CTG TCC GCT ACT TAC AAA CTG TCC CAT CCG G	23 23 37	23 24 25
Gln ²⁶ ->Ala ²⁶ Gln ¹⁷⁴ ->Ala ¹⁷⁴ Arg ¹⁷⁰ ->Ala ¹⁷⁰ Arg ¹⁶⁷ ->Ala ¹⁶⁷	TTC GTA AAA TCG CGG GTG ACG G TCA TCT GGC TGC GCC GTA ATA G CCG TGT TCT GGC TCA TCT GGC T GAA GTA TCT TAC GCT GTT CTG CGT	22 22 22 24	26 27 28 29
Deletion 167 Lys ⁴¹ ->Ala ⁴¹ His ⁴⁴ ->Lys ⁴⁴ Glu ⁴⁷ ->Ala ⁴⁷	GAA GTA TCT TAC TAA GTT CTG CGT C CGC TAC TTA CCG ACT GTG CCA T CAA ACT GTG CAA GCC GGA AGA G CAT CCG GAA GCA CTG GTA CTG C	25 22 22 22	30 31 32 33

Table 2 (cont.)

G-CSE ANALOGS	SEQUENCES(5'→3')	Length(nucleotide)	Seq. ID
Arg23→Ala23	GGA ACA GGT TGC TAA AAT CCA GG	23	34
Lys24→Ala24	GAA CAG GTT CGT GCG ATC CAG GGT G	25	35
Glu20→Ala20	GAA ATG TCT GGC ACA GGT TCG T	22	36
Asp28→Ala28	TCC AGG GTG CCG GTG CTG C	19	37
Met127→Glu127	AAG AGC TCG GTG AGG CAC CAG CT	23	38
Met138→Glu138	CTC AAG GTG CTG AGC CGG CAT TC	23	39
Met127→Leu127	GAG CTC GGT CTG GCA CCA GC	20	40
Met138→Leu138	TCA AGG TGC TCT GCC GGC ATT	21	41
Ser13→Ala13	TCT GCC GCA AGC CTT TCT GCT GA	23	42
Lys17→Ala17	CTT TCT GCT GGC ATG TCT GGA ACA	24	43
Gln121→Ala121	CTA TTT GGC AAG CGA TGG AAG AGC	24	44
Glu124→Ala124	CAG ATG GAA GCG CTC GGT ATG	21	45

Table 2 (con'tl)

G-CSF ANALOGS	SEQUENCES(5'→3')	Length(nucleotide)	Seq. ID
Met ^{127,138} → Leu ^{127,138}	GAG CTC GGT CTG GCA CCA GC TCA AGG TGC TCT GCC GGC ATT	20 21	46 47
**Glu ²⁰ →Ala ²⁰ ; Ser ¹³ →Gly ¹³	GAA ATG TCT GGC ACA GGT TCG T	22	48

** This analog came about during the preparation of G-CSF analog Glu²⁰→Ala²⁰. As several clones were being sequenced to identify the Glu²⁰→Ala²⁰ analog, the Glu²⁰→Ala²⁰; Ser¹³→Gly¹³ analog was identified. This double mutant was the result of an in vitro Klenow DNA polymerase reaction mistake.

55 D. Preparation of G-CSF Analogs Using DNA Amplification

This example relates to methods for producing G-CSF analogs using a DNA amplification technique. Essentially, DNA encoding each analog was amplified in two separate pieces, combined, and then the total

sequence itself amplified. Depending upon where the desired change in the original G-CSF DNA was to be made, internal primers were used to incorporate the change, and generate the two separate amplified pieces. For example, for amplification of the 5' end of the desired analog DNA, a 5' flanking primer (complementary to a sequence of the plasmid upstream from the G-CSF original DNA) was used at one end of the region to be amplified, and an internal primer, capable of hybridizing to the original DNA but incorporating the desired change, was used for priming the other end. The resulting amplified region stretched from the 5' flanking primer through the internal primer. The same was done for the 3' terminus, using a 3' flanking primer (complementary to a sequence of the plasmid downstream from the G-CSF original DNA) and an internal primer complementary to the region of the intended mutation. Once the two "halves" (which may or may not be equal in size, depending on the location of the internal primer) were amplified, the two "halves" were allowed to connect. Once connected, the 5' flanking primer and the 3' flanking primer were used to amplify the entire sequence containing the desired change.

If more than one change is desired, the above process may be modified to incorporate the change into the internal primer, or the process may be repeated using a different internal primer. Alternatively, the gene amplification process may be used with other methods for creating changes in nucleic acid sequence, such as the phage based mutagenesis technique as described above. Examples of process for preparing analogs with more than one change are described below.

To create the G-CSF analogs described below, the template DNA used was the sequence as in FIGURE 1 plus certain flanking regions (from a plasmid containing the G-CSF coding region). These flanking regions were used as the 5' and 3' flanking primers and are set forth below. The amplification reactions were performed in 40 μ l volumes containing 10 mM Tris-HCl, 1.5 mM MgCl₂, 50 mM KCl, 0.1 mg/ml gelatin, pH 8.3 at 20°C. The 40 μ l reactions also contained 0.1mM of each dNTP, 10 pmoles of each primer, and 1 ng of template DNA. Each amplification was repeated for 15 cycles. Each cycle consisted of 0.5 minutes at 94°C, 0.5 minutes at 50°C, and 0.75 minutes at 72°C. Flanking primers were 20 nucleotides in length and internal primers were 20 to 25 nucleotides in length. This resulted in multiple copies of double stranded DNA encoding either the front portion or the back portion of the desired G-CSF analog.

For combining the two "halves," one fortieth of each of the two reactions was combined in a third DNA amplification reaction. The two portions were allowed to anneal at the internal primer location, as their ends bearing the mutation were complementary, and following a cycle of polymerization, give rise to a full length DNA sequence. Once so annealed, the whole analog was amplified using the 5' and 3' flanking primers. This amplification process was repeated for 15 cycles as described above.

The completed, amplified analog DNA sequence was cleaved with XbaI and XhoI restriction endonuclease to produce cohesive ends for insertion into a vector. The cleaved DNA was placed into a plasmid vector, and that vector was used to transform *E. coli*. Transformants were challenged with kanamycin at 50 μ g/ml and incubated at 30°C. Production of G-CSF analog protein was confirmed by polyacrylamide gel electrophoresis of a whole cell lysate. The presence of the desired mutation was confirmed by DNA sequence analysis of plasmid purified from the production isolate. Cultures were then grown, and cells were harvested, and the G-CSF analogs were purified as set forth below.

Set forth below in Table 3 are the specific primers used for each analog made using gene amplification.

Table 3

Analog Seq. ID	Internal Primer(5'→3')	
His ⁴⁴ →Ala ⁴⁴	5'primer-TTCCGGAGCGCACAGTTTG	49
	3'primer-CAAACGTGGGCTCCGGAAGAGC	50
Thr ¹¹⁷ →Ala ¹¹⁷	5'primer-ATGCCAAATGCAGTAGCAAAG	51
	3'primer-CTTTGCTACTGCAATTTGGCAACA	52
Asp ¹¹⁰ →Ala ¹¹⁰	5'primer-ATCAGCTACTGCTAGCTGCAGA	53
	3'primer-TCTGCAGCTAGCAGTAGCTGACT	54
Gln ²¹ →Ala ²¹	5'primer-TTACGAACCGCTCCAGACATT	55
	3'primer-AATGCTCTGGAAGCGGTTCTGTAATAAT	56
Asp ¹¹³ →Ala ¹¹³	5'primer-GTAGCAATGCAGCTACATCTA	57
	3'primer-TAGATGTAGCTGCATTTGCTACTAC	58
His ⁵³ →Ala ⁵³	5'primer-CCAAGAGAAGCACCCAGCAG	59
	3'primer-CTGCTGGTGCCTCTCTTGGGA	60
For each analog, the following 5' flanking primer was used:		
5'-CACTGGCGGTGATAATGAGC		61
For each analog, the following 3' flanking primer was used:		
3'-GGTCATTACGACCGGATC		62

1. Construction of Double Mutation

To make G-CSF analog Gln^{12,21}→Glu^{12,21}, two separate DNA amplifications were conducted to create the two DNA mutations. The template DNA used was the sequence as in FIGURE 1 plus certain flanking regions (from a plasmid containing the G-CSF coding region). The precise sequences are listed below. Each of the two DNA amplification reactions were carried out using a Perkin Elmer/Cetus DNA Thermal Cycler. The 40 μ l reaction mix consisted of 1X PCR Buffer (Cetus), 0.2 mM each of the 4 dNTPs (Cetus), 50 pmol of each primer oligonucleotide, 2 ng of G-CSF template DNA (on a plasmid vector), and 1 unit of Taq polymerase (Cetus). The amplification process was carried out for 30 cycles. Each cycle consisted of 1 minute at 94 °C, 2 minutes at 50 °C, and 3 minutes at 72 °C.

DNA amplification "A" used the oligonucleotides:

5' CCACTGGCGGTGATACTGAGC 3' (Seq. ID 63) and
 40 5' AGCAGAAAGCTTTCCGGCAGAGAAGAAGCAGGA 3' (Seq. ID 64)
 DNA amplification "B" used the oligonucleotides: 5' GCCGCAAAGCTTTCTGCTGAAATGCTGTG-
 GAAGAGGTTTCGTAAATCCAGGGTGA 3' (Seq. ID 65) and
 5' CTGGAATGCAGAAGCAAATGCCGGCATAGCACCTTCAGTCGGTTGCAGAGCTGGTGCCA 3' (Seq. ID 66)

45 From the 109 base pair double stranded DNA product obtained after DNA amplification "A", a 64 base pair XbaI to HindIII DNA fragment was cut and isolated that contained the DNA mutation Gln¹²→Glu¹². From the 509 base pair double stranded DNA product obtained after DNA amplification "B", a 197 base pair HindIII to BsmI DNA fragment was cut and isolated that contained the DNA mutation Gln²¹→Glu²¹.

The "A" and "B" fragments were ligated together with a 4.8 kilo-base pair XbaI to BsmI DNA plasmid vector fragment. The ligation mix consisted of equal molar DNA restriction fragments, ligation buffer (25 mM Tris-HCl pH 7.8, 10 mM MgCl₂, 2 mM DTT, 0.5 mM rATP, and 100 μ g/ml BSA) and T4 DNA ligase and was incubated overnight at 14 °C. The ligated DNA was then transformed into *E. coli* FM5 cells by electroporation using a Bio Rad Gene Pulsar apparatus (BioRad, Richmond, CA). A clone was isolated and the plasmid construct verified to contain the two mutations by DNA sequencing. This 'intermediate' vector also
 55 contained a deletion of a 193 base pair BsmI to BsmI DNA fragment. The final plasmid vector was constructed by ligation and transformation (as described above) of DNA fragments obtained by cutting and isolating a 2 kilo-base pair SstI to BamHI DNA fragment from the intermediate vector, a 2.8 kbp SstI to EcoRI DNA fragment from the plasmid vector, and a 360 bp BamHI to EcoRI DNA fragment from the

plasmid vector. The final construct was verified by DNA sequencing the G-CSF gene. Cultures were grown, and the cells were harvested, and the G-CSF analogs were purified as set forth below.

As indicated above, any combination of mutagenesis techniques may be used to generate a G-CSF analog nucleic acid (and expression product) having one or more than one alteration. The two examples above, using M13-based mutagenesis and gene amplification-based mutagenesis, are illustrative.

E. Expression of G-CSF Analog DNA

The G-CSF analog DNAs were then placed into a plasmid vector and used to transform *E. coli* strain FM5 (ATCC#53911). The present G-CSF analog DNAs contained on plasmids and in bacterial host cells are available from the American Type Culture Collection, Rockville, MD, and the accession designations are indicated below.

One liter cultures were grown in broth containing 10g tryptone, 5g yeast extract and 5g NaCl) at 30°C until reaching a density at A₆₀₀ of 0.5, at which point they were rapidly heated to 42°C. The flasks were allowed to continue shaking at for three hours.

Other prokaryotic or eukaryotic host cells may also be used, such as other bacterial cells, strains or species, mammalian cells in culture (COS, CHO or other types) insect cells or multicellular organs or organisms, or plant cells or multicellular organs or organisms, and a skilled practitioner will recognize the appropriate host. The present G-CSF analogs and related compositions may also be prepared synthetically, as, for example, by solid phase peptide synthesis methods, or other chemical manufacturing techniques. Other cloning and expression systems will be apparent to those skilled in the art.

F. Purification of G-CSF Analog Protein

Cells were harvested by centrifugation (10,000 x G, 20 minutes, 4°C). The pellet (usually 5 grams) was resuspended in 30 ml of 1mM DTT and passed three times through a French press cell at 10,000 psi. The broken cell suspension was centrifuged at 10,000g for 30 minutes, the supernatant removed, and the pellet resuspended in 30-40 ml water. This was recentrifuged at 10,000 x G for 30 minutes, and this pellet was dissolved in 25 ml of 2% Sarkosyl and 50mM Tris at pH 8. Copper sulfate was added to a concentration of 40μM, and the mixture was allowed to stir for at least 15 hours at 15-25°C. The mixture was then centrifuged at 20,000 x G for 30 minutes. The resultant solubilized protein mixture was diluted four-fold with 133 mM Tris, pH 7.7, the Sarkosyl was removed, and the supernatant was then applied to a DEAE-cellulose (Whatman DE-52) column equilibrated in 20mM Tris, pH 7.7. After loading and washing the column with the same buffer, the analogs were eluted with 20mM Tris /NaCl (between 35mM to 100mM depending on the analog, as indicated below), pH 7.7. For most of the analogs, the eluent from the DEAE column was adjusted to a pH of 5.4, with 50% acetic acid and diluted as necessary (to obtain the proper conductivity) with 5mM sodium acetate pH 5.4. The solution was then loaded onto a CM-sepharose column equilibrated in 20 mM sodium acetate, pH 5.4. The column was then washed with 20mM NaAc, pH 5.4 until the absorbance at 280 nm was approximately zero. The G-CSF analog was then eluted with sodium acetate/NaCl in concentrations as described below in Table 4. The DEAE column eluents for those analogs not applied to the CM-sepharose column were dialyzed directly into 10mM NaAc, pH 4.0 buffer. The purified G-CSF analogs were then suitably isolated for *in vitro* analysis. The salt concentrations used for eluting the analogs varied, as noted above. Below, the salt concentrations for the DEAE cellulose column and for the CM-sepharose column are listed:

Table 4
Salt Concentrations

	<u>Analog</u>	<u>DEAE Cellulose</u>	<u>CM-Sepharose</u>
5	Lys17->Arg17	35mM	37.5mM
10	Lys24->Arg24	35mM	37.5mM
	Lys35->Arg35	35mM	37.5mM
	Lys41->Arg41	35mM	37.5mM
15	Lys17, 24, 35->Arg17, 24, 35	35mM	37.5mM
	Lys17, 35, 41->Arg17, 35, 41	35mM	37.5mM

Table 4 Con't

	<u>Analog</u>	<u>DEAE Cellulose</u>	<u>CM-Sepharose</u>
5	Lys24, 35, 41-	35mM	37.5mM
	>Arg24, 35, 41		
10	Lys17, 24, 35, 41	35mM	37.5mM
	->Arg17, 24, 35, 41		
	Lys17, 24, 41-	35mM	37.5mM
	>Arg17, 24, 41		
15	Gln68->Glu68	60mM	37.5mM
	Cys37, 43->Ser37, 43	40mM	37.5mM
	Gln26->Ala26	40mM	40mM
20	Gln174->Ala174	40mM	40mM
	Arg170->Ala170	40mM	40mM
	Arg167->Ala167	40mM	40mM
	Deletion 167*	N/A	N/A
25	Lys41->Ala41	160mM	40mM
	His44->Lys44	40mM	60mM
	Glu47->Ala47	40mM	40mM
30	Arg23->Ala23	40mM	40mM
	Lys24->Ala24	120mM	40mM
	Glu20->Ala20	40mM	60mM
35	Asp28->Ala28	40mM	80mM
	Met127->Glu127	80mM	40mM
	Met138->Glu138	80mM	40mM
	Met127->Leu127	40mM	40mM
40	Met138->Leu138	40mM	40mM
	Cys18->Ala18	40mM	37.5mM
	Gln12, 21->Glu12, 21	60mM	37.5mM
45	Gln12, 21, 68-	60mM	37.5mM
	>Glu12, 21, 68		
	Glu20->Ala20;		
	Ser13		
50	->Gly13	40mM	80mM

55

Table 4 Con't

	<u>Analog</u>	<u>DEAE Cellulose</u>	<u>CM-Sephadex</u>
5	Met127, 138-	40mM	40mM
	>Leu127, 138		
10	Ser13->Ala13	40mM	40mM
	Lys17->Ala17	80mM	40mM
	Gln121->Ala121	40mM	60mM
15	Gln21->Ala21	50mM	Gradient 0 -150mM
	His44->Ala44**	40mM	N/A
	His53->Ala53**	50mM	N/A
	Asp110->Ala110**	40mM	N/A
20	Asp113->Ala113**	40mM	N/A
	Thr117->Ala117**	50mM	N/A
	Asp28->Ala28;	50mM	N/A
25	Asp110		
	Ala110**		
	Glu124->Ala124**	40mM	40mM

* For Deletion 167, the data are unavailable.

** For these analogs, the DEAE cellulose column alone was used for purification.

The above purification methods are illustrative, and a skilled practitioner will recognize that other means are available for obtaining the present G-CSF analogs.

G. Biological Assays

Regardless of which methods were used to create the present G-CSF analogs, the analogs were subject to assays for biological activity. Tritiated thymidine assays were conducted to ascertain the degree of cell division. Other biological assays, however, may be used to ascertain the desired activity. Biological assays such as assaying for the ability to induce terminal differentiation in mouse WEHI-3B (D+) leukemic cell line, also provides indication of G-CSF activity. See Nicola, et al., Blood 54: 614-27 (1979). Other *in vitro* assays may be used to ascertain biological activity. See Nicola, Annu. Rev. Biochem. 58: 45-77 (1989). In general, the test for biological activity should provide analysis for the desired result, such as increase or decrease in biological activity (as compared to non-altered G-CSF), different biological activity (as compared to non-altered G-CSF), receptor affinity analysis, or serum half-life analysis. The list is incomplete, and those skilled in the art will recognize other assays useful for testing for the desired end result.

The ³H-thymidine assay was performed using standard methods. Bone marrow was obtained from sacrificed female Balb C mice. Bone marrow cells were briefly suspended, centrifuged, and resuspended in a growth medium. A 160 ul aliquot containing approximately 10,000 cells was placed into each well of a 96 well micro-titer plate. Samples of the purified G-CSF analogs (as prepared above) were added to each well, and incubated for 68 hours. Tritiated thymidine was added to the wells and allowed to incubate for 5 additional hours. After the 5 hour incubation time, the cells were harvested, filtered, and thoroughly rinsed. The filters were added to a vial containing scintillation fluid. The beta emissions were counted (LKB Betaplate scintillation counter). Standards and analogs were analyzed in triplicate, and samples which fell substantially above or below the standard curve were re-assayed with the proper dilution. The results

reported here are the average of the triplicate analog data relative to the unaltered recombinant human G-CSF standard results.

H. HPLC Analysis

High pressure liquid chromatography was performed on purified samples of analog. Although peak position on a reverse phase HPLC column is not a definitive indication of structural similarity between two proteins, analogs which have similar retention times may have the same type of hydrophobic interactions with the HPLC column as the non-altered molecule. This is one indication of an overall similar structure.

Samples of the analog and the non-altered recombinant human G-CSF were analyzed on a reverse phase (0.46 x 25 cm) Vydac 214TP54 column (Separations Group, Inc. Hesperia, CA). The purified analog G-CSF samples were prepared in 20 mM acetate and 40 mM NaCl solution buffered at pH 5.2 to a final concentration of 0.1 mg/ml to 5 mg/ml, depending on how the analog performed in the column. Varying amounts (depending on the concentration) were loaded onto the HPLC column, which had been equilibrated with an aqueous solution containing 1% isopropanol, 52.8% acetonitrile, and .38% trifluoro acetate (TFA). The samples were subjected to a gradient of 0.86%/minute acetonitrile, and .002% TFA.

I. Results

Presented below are the results of the above biological assays and HPLC analysis. Biological activity is the average of triplicate data and reported as a percentage of the control standard (non-altered G-CSF). Relative HPLC peak position is the position of the analog G-CSF relative to the control standard (non-altered G-CSF) peak. The "+" or "-" symbols indicate whether the analog HPLC peak was in advance of or followed the control standard peak (in minutes). Not all of the variants had been analyzed for relative HPLC peak, and only those so analyzed are included below. Also presented are the American Type Culture Collection designations for E. coli host cells containing the nucleic acids coding for the present analogs, as prepared above.

Table 5

Seq. ID	Variant	Analogue	Relative HPLC Peak	ATCC No.	% Normal G-CSF Activity
67	1	Lys17->Arg17	N/A	69184	N/A
68	2	Lys24->Arg24	N/A	69185	N/A
69	3	Lys35->Arg35	N/A	69186	N/A
70	4	Lys41->Arg41	N/A	69187	N/A
71	5	Lys17,24,35->Arg17,24,35	N/A	69189	N/A
72	6	Lys17,35,41->Arg17,35,41	N/A	69192	N/A
73	7	Lys24,35,41->Arg24,35,41	N/A	69191	N/A
74	8	Lys17,24,35,41 ->Arg17,24,35,41	N/A	69193	N/A
75	9	Lys17,24,41->Arg17,24,41	N/A	69190	N/A
76	10	Gln68->Glu68	N/A	69196	N/A
77	11	Cys37,43->Ser37,43	N/A	69197	N/A
78	12	Gln26->Ala26	+ .96	69201	51%
79	13	Gln174->Ala174	+ .14	69202	100%
80	14	Arg170->Ala170	+ .78	69203	100%

Table 5 Cont'd

Seq. ID	Variant	Analog	Relative HPLC Peak	ATCC No.	% Normal G-CSF Activity
81	15	Arg167->Ala167	+ .54	69204	110%
82	16	Deletion 167	- .39	69207	N/A
83	17	Lys41->Ala41	+ .25	69208	81%
84	18	His44->Lys44	-1.53	69212	70%
85	19	Glu47->Ala47	+ .14	69205	0%
86	20	Arg23->Ala23	- .03	69206	31%
87	21	Lys24->Ala24	+1.95	69213	0%
88	22	Glu20->Ala20	-0.07	69211	0%
89	23	Asp28->Ala28	- .30	69210	147%
90	24	Met127->Glu127	N/A	69223	N/A
91	25	Met138->Glu138	N/A	69222	N/A
92	26	Met127->Leu127	N/A	69198	N/A
93	27	Met138->Leu138	N/A	69199	N/A
94	28	Cys18->Ala18	N/A	69188	N/A
95	29	Gln12,21->Glu12,21	N/A	69194	N/A
96	30	Gln12,21,68->Glu12,21,68	N/A	69195	N/A
97	31	Glu20->Ala20; Ser13	+1.74	69209	0%

Table 5. Con't

Seq. ID	Variant	Analog	Relative HPLC Peak	ATCC No.	% Normal G-CSF Activity
		->Gly ¹³			
98	32	Met ^{127,138} ->Leu ^{127,138}	+1.43	69200	98%
99	33	Ser ¹³ ->Ala ¹³	0	69221	110%
100	34	Lys ¹⁷ ->Ala ¹⁷	+0.50	69226	70%
101	35	Gln ¹²¹ ->Ala ¹²¹	+2.7	69225	100%
102	36	Gln ²¹ ->Ala ²¹	+0.63	69217	9.6%
103	37	His ⁴⁴ ->Ala ⁴⁴	+1.52	69215	10.8%
104	38	His ⁵³ ->Ala ⁵³	+0.99	69219	8.3%
105	39	Asp ¹¹⁰ ->Ala ¹¹⁰	+1.97	69216	29%
106	40	Asp ¹¹³ ->Ala ¹¹³	-0.34	69218	0%
107	41	Thr ¹¹⁷ ->Ala ¹¹⁷	+0.4	69214	9.7%
108	42	Asp ²⁸ ->Ala ²⁸ ; Asp ¹¹⁰ Ala ¹¹⁰	+3.2	69220	20.6%

Table 5 Con't

Seq. ID	Variant	Analog	Relative HPLC Peak	ATCC No.	% Normal G-CSF Activity
109	43	Glu124->Ala124	+0.16	69224	75%
110	44	Phe114->Val 114, Thr117->Ala 117**	+0.53		0%

**This analog was apparently a result of an inadvertent error in the oligo which was used to prepare number 41, above (Thr117->Ala 117), and thus was prepared identically to the process used for that analog.

"N/A" indicates data which are not available.

1. Identification of Structure-Function Relationships

The first step used to design the present analogs was to determine what moieties are necessary for structural integrity of the G-CSF molecule. This was done at the amino acid residue level, although the

atomic level is also available for analysis. Modification of the residues necessary for structural integrity results in change in the overall structure of the G-CSF molecule. This may or may not be desirable, depending on the analog one wishes to produce. The working examples here were designed to maintain the overall structural integrity of the G-CSF molecule, for the purpose of maintain G-CSF receptor binding of the analog to the G-CSF receptor (as used in this section below, the "G-CSF receptor" refers to the natural G-CSF receptor, found on hematopoietic cells). It was assumed, and confirmed by the studies presented here, that G-CSF receptor binding is a necessary step for at least one biological activity, as determined by the above biological assays.

As can be seen from the figures, G-CSF (here, recombinant human met-G-CSF) is an antiparallel 4- α helical bundle with a left-handed twist, and with overall dimensions of 45 Å x 30 Å x 24 Å. The four helices within the bundle are referred to as helices A, B, C and D, and their connecting loops are known as the AB, BC and CD loops. The helix crossing angles range from -167.5° to -159.4°. Helices A, B, and C are straight, whereas helix D contains two kinds of structural characteristics, at Gly 150 and Ser 160 (of the recombinant human met-G-CSF). Overall, the G-CSF molecule is a bundle of four helices, connected in series by external loops. This structural information was then correlated with known functional information. It was known that residues (including methionine at position 1) 47, 23, 24, 20, 21, 44, 53, 113, 110, 28 and 114 may be modified, and the effect on biological activity would be substantial.

The majority of single mutations which lowered biological activity were centered around two regions of G-CSF that are separated by 30 Å, and are located on different faces of the four helix bundle. One region involves interactions between the A helix and the D helix. This is further confirmed by the presence of salt bridges in the non-altered molecule as follows:

Atom	Helix	Atom	Helix	Distance
Arg 170 N1	D	Tyr 166 OH	A	3.3
Tyr 166 OH	D	Arg 23 N2	A	3.3
Glu 163 OE1	D	Arg 23 N1	A	2.8
Arg 23 N1	A	Gln 26 OE1	A	3.1
Gln 159 NE2	D	Gln 26 O	A	3.3

Distances reported here were for molecule A, as indicated in FIGURE 5 (wherein three G-CSF molecules crystallized together and were designated as A, B, and C). As can be seen, there is a web of salt bridges between helix A and helix D, which act to stabilize the helix A structure, and therefore affect the overall structure of the G-CSF molecule.

The area centering around residues Glu 20, Arg 23 and Lys 24 are found on the hydrophilic face of the A helix (residues 20-37). Substitution of the residues with the non-charged alanine residue at positions 20 and 23 resulted in similar HPLC retention times, indicating similarity in structure. Alteration of these sites altered the biological activity (as indicated by the present assays). Substitution at Lys 24 altered biological activity, but did not result in a similar HPLC retention time as the other two alterations.

The second site at which alteration lowered biological activity involves the AB helix. Changing glutamine at position 47 to alanine (analog no. 19, above) reduced biological activity (in the thymidine uptake assay) to zero. The AB helix is predominantly hydrophobic, except at the amino and carboxy termini; it contains one turn of a 3¹⁰ helix. There are two histidines at each termini (His 44 and His 56) and an additional glutamate at residue 46 which has the potential to form a salt bridge to His 44. The Fourier transformed infra red spectrographic analysis (FTIR) of the analog suggests this analog is structurally similar to the non-altered recombinant G-CSF molecule. Further testing showed that this analog would not crystallize under the same conditions as the non-altered recombinant molecule.

Alterations at the carboxy terminus (Gln 174, Arg 167 and Arg 170) had little effect on biological activity. In contrast, deletion of the last eight residues (167-175) lowered biological activity. These results may indicate that the deletion destabilizes the overall structure which prevents the mutant from proper binding to the G-CSF receptor (and thus initiating signal transduction).

Generally, for the G-CSF internal core – the internal four helix bundle lacking the external loops – the hydrophobic internal residues are essential for structural integrity. For example, in helix A, the internal hydrophobic residues are (with methionine being position 1) Phe 14, Cys 18, Val 22, Ile 25, Ile 32 and Leu 36. Generally, for the G-CSF internal core – the internal four helix bundle lacking the external loops – the hydrophobic internal residues are essential for structural integrity. For example, in helix A, the internal hydrophobic residues are (with methionine being position 1 as in FIGURE 1) Phe 14, Cys 18, Val 22, Ile 25, Ile 32 and Leu 36. The other hydrophobic residues (again with the met at position 1) are: helix B, Ala 72,

Leu 76, Leu 79, Leu 83, Tyr 86, Leu 90 Leu 93; helix C, Leu 104, Leu 107, Val 111, Ala 114, Ile 118, Met 122; and helix D, Val 154, Val 158, Phe 161, Val 164, Val 168, Leu 172.

The above biological activity data, from the presently prepared G-CSF analogs, demonstrate that modification of the external loops interfere least with G-CSF overall structure. Preferred loops for analog preparation are the AB loop and the CD loop. The loops are relatively flexible structures as compared to the helices. The loops may contribute to the proteolysis of the molecule. G-CSF is relatively fast acting *in vivo* as the purpose the molecule serves is to generate a response to a biological challenge, i.e., selectively stimulate neutrophils. The G-CSF turnover rate is also relatively fast. The flexibility of the loops may provide a "handle" for proteases to attach to the molecule to inactivate the molecule. Modification of the loops to prevent protease degradation, yet have (via retention of the overall structure of non-modified G-CSF) no loss in biological activity may be accomplished.

This phenomenon is probably not limited to the G-CSF molecule but may also be common to the other molecules with known similar overall structures, as presented in Figure 2. Alteration of the external loop, for example hGH, Interferon B, IL-2, GM-CSF and IL-4 may provide the least change to the overall structure. The external loops on the GM-CSF molecule are not as flexible as those found on the G-CSF molecule, and this may indicate a longer serum life, consistent with the broader biological activity of GM-CSF. Thus, the external loops of G-CSF may be modified by releasing the external loops from the beta-sheet structure, which may make the loops more flexible (similar to those G-CSF) and therefore make the molecule more susceptible to protease degradation (and thus increase the turnover rate).

Alteration of these external loops may be effected by stabilizing the loops by connection to one or more of the internal helices. Connecting means are known to those in the art, such as the formation of a beta sheet, salt bridge, disulfide bonding or hydrophobic interactions, and other means are available. Also, deletion of one or more moieties, such as one or more amino acid residues or portions thereof, to prepare an abbreviated molecule and thus eliminate certain portions of the external loops may be effected.

Thus, by alteration of the external loops, preferably the AB loop (amino acids 58-72 of r-hu-met G-CSF) or the CD loop (amino acids 119 to 145 of r-hu-met G-CSF), and less preferably the amino terminus (amino acids 1-10), one may therefore modify the biological function without elimination of G-CSF G-CSF receptor binding. For example, one may: (1) increase half-life (or prepare an oral dosage form, for example) of the G-CSF molecule by, for example, decreasing the ability of proteases to act on the G-CSF molecule or adding chemical modifications to the G-CSF molecule, such as one or more polyethylene glycol molecules or enteric coatings for oral formulation which would act to change some characteristic of the G-CSF molecule as described above, such as increasing serum or other half-life or decreasing antigenicity; (2) prepare a hybrid molecule, such as combining G-CSF with part or all of another protein such as another cytokine or another protein which effects signal transduction via entry through the cell through a G-CSF G-CSF receptor transport mechanism; or (3) increase the biological activity as in, for example, the ability to selectively stimulate neutrophils (as compared to a non-modified G-CSF molecule). This list is not limited to the above exemplars.

Another aspect observed from the above data is that stabilizing surface interactions may affect biological activity. This is apparent from comparing analogs 23 and 40. Analog 23 contains a substitution of the charged asparagine residue at position 28 for the neutrally-charged alanine residue in that position, and such substitution resulted in a 50% increase in the biological activity (as measured by the disclosed thymidine uptake assays). The asparagine residue at position 28 has a surface interaction with the asparagine residue at position 113; both residues being negatively charged, there is a certain amount of instability (due to the repelling of like charged moieties). When, however the asparagine at position 113 is replaced with the neutrally-charged alanine, the biological activity drops to zero (in the present assay system). This indicates that the asparagine at position 113 is critical to biological activity, and elimination of the asparagine at position 28 serves to increase the effect that asparagine at position 113 possesses.

The domains required for G-CSF receptor binding were also determined based on the above analogs prepared and the G-CSF structure. The G-CSF receptor binding domain is located at residues (with methionine being position 1) 11-57 (between the A and AB helix) and 100-118 (between the B and C helices). One may also prepare abbreviated molecules capable of binding to a G-CSF receptor and initiate signal transduction for selectively stimulating neutrophils by changing the external loop structure and having the receptor binding domains remain intact.

Residues essential for biological activity and presumably G-CSF receptor binding or signal transduction have been identified. Two distinct sites are located on two different regions of the secondary structure. What is here called "Site A" is located on a helix which is constrained by salt bridge contacts between two other members of the helical bundle. The second site, "Site B" is located on a relatively more flexible helix, AB. The AB helix is potentially more sensitive to local pH changes because of the type and position of the

residues at the carboxy and amino termini. The functional importance of this flexible helix may be important in a conformationally induced fit when binding to the G-CSF receptor. Additionally, the extended portion of the D helix is also indicated to be a G-CSF receptor binding domain, as ascertained by direct mutational and indirect comparative protein structure analysis. Deletion of the carboxy terminal end of r-hu-met-G-CSF reduces activity as it does for hGH, see, Cunningham and Wells, Science 244: 1081-1084 (1989). Cytokines which have similar structures, such as IL-6 and GM-CSF with predicted similar topology also center their biological activity along the carboxy end of the D helix, see Bazan, Immunology Today 11: 350-354 (1990).

A comparison of the structures and the positions of G-CSF receptor binding determinants between G-CSF and hGH suggests both molecules have similar means of signal transduction. Two separate G-CSF receptor binding sites have been identified for hGH De Vos et al., Science 255: 306-32 (1991). One of these binding sites (called "Site I") is formed by residues on the exposed faces of hGH's helix 1, the connection region between helix 1 and 2, and helix 4. The second binding site (called "Site II") is formed by surface residues of helix 1 and helix 3.

The G-CSF receptor binding determinants identified for G-CSF are located in the same relative positions as those identified for hGH. The G-CSF receptor binding site located in the connecting region between helix A and B on the AB helix (Site A) is similar in position to that reported for a small piece of helix (residues 38-47) of hGH. A single point mutation in the AB helix of G-CSF significantly reduces biological activity (as ascertained in the present assays), indicating the role in a G-CSF receptor-ligand interface. Binding of the G-CSF receptor may destabilize the 3¹⁰ helical nature of this region and induce a conformation change improving the binding energy of the ligand/G-CSF receptor complex.

In the hGH receptor complex, the first helix of the bundle donates residues to both of the binding sites required to dimerize the hGH receptor. Mutational analysis of the corresponding helix of G-CSF (helix A) has identified three residues which are required for biological activity. Of these three residues, Glu 20 and Arg 24 lie on one face of the helical bundle towards helix C, whereas the side chain of Arg 23 (in two of the three molecules in the asymmetric unit) points to the face of the bundle towards helix D. The position of side chains of these biologically important residues indicates that similar to hGH, G-CSF may have a second G-CSF receptor binding site along the interface between helix A and helix C. In contrast with the hGH molecule, the amino terminus of G-CSF has a limited biological role as deletion of the first 11 residues has little effect on the biological activity.

As indicated above (see FIGURE 2, for example), G-CSF has a topological similarity with other cytokines. A correlation of the structure with previous biochemical studies, mutational analysis and direct comparison of specific residues of the hGH receptor complex indicates that G-CSF has two receptor binding sites. Site A lies along the interface of the A and D helices and includes residues in the small AB helix. Site B also includes residues in the A helix but lies along the interface between helices A and C. The conservation of structure and relative positions of biologically important residues between G-CSF and hGH is one indication of a common method of signal transduction in that the receptor is bound in two places. It is therefore found that G-CSF analogs possessing altered G-CSF receptor binding domains may be prepared by alteration at either of the G-CSF receptor binding sites (residues 20-57 and 145-175).

Knowledge of the three dimensional structure and correlation of the composition of G-CSF protein makes possible a systematic, rational method for preparing G-CSF analogs. The above working examples have demonstrated that the limitations of the size and polarity of the side chains within the core of the structure dictate how much change the molecule can tolerate before the overall structure is changed.

SEQUENCE LISTING

(1) GENERAL INFORMATION:

(i) APPLICANT: Amgen Inc.

(ii) TITLE OF INVENTION: G-CSF ANALOG COMPOSITIONS AND METHODS

(iii) NUMBER OF SEQUENCES: 110

(iv) CORRESPONDENCE ADDRESS:

(A) ADDRESSEE: Amgen Inc.

(B) STREET: Amgen Center, 1840 DeHavilland Drive

(C) CITY: Thousand Oaks

(D) STATE: California

(E) COUNTRY: United States of America

(F) ZIP: 91320-1789

(v) COMPUTER READABLE FORM:

(A) MEDIUM TYPE: Floppy disk

(B) COMPUTER: IBM PC compatible

(C) OPERATING SYSTEM: PC-DOS/MS-DOS

(2) INFORMATION FOR SEQ ID NO:1:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 565 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:

(A) NAME/KEY: CDS

(B) LOCATION: 30..554

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

TCTAGAAAAA	ACCAAGGAGG	TAATAAATA	ATG	ACT	CCA	TTA	GGT	CCT	GCT	TCT	53
			Met	Thr	Pro	Leu	Gly	Pro	Ala	Ser	
			1				5				

TCT	CTG	CCG	CAA	AGC	TTT	CTG	CTG	AAA	TGT	CTG	GAA	CAG	GIT	CGT	AAA	101
Ser	Leu	Pro	Gln	Ser	Phe	Leu	Leu	Lys	Cys	Leu	Glu	Gln	Val	Arg	Lys	
	10					15				20						

ATC	CAG	GGT	GAC	GGT	GCT	GCA	CTG	CAA	GAA	AAA	CTG	TGC	GCT	ACT	TAC	149
Ile	Gln	Gly	Asp	Gly	Ala	Ala	Leu	Gln	Glu	Lys	Leu	Cys	Ala	Thr	Tyr	
	25				30				35					40		

EP 0 612 846 A1

AAA CTG TGC CAT CCG GAA GAG CTG GTA CTG CTG GGT CAT TCT CTT GGG 197
 Lys Leu Cys His Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly 55
 45
 5 ATC CCG TGG GCT CCG CTG TCT TCT TGT CCA TCT CAA GCT CTT CAG CTG 245
 Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu 60
 65 70
 GCT GGT TGT CTG TCT CAA CTG CAT TCT GGT CTG TTC CTG TAT CAG GGT 293
 Ala Gly Cys Leu Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly 75
 80 85
 10 CTT CTG CAA GCT CTG GAA GGT ATC TCT CCG GAA CTG GGT CCG ACT CTG 341
 Leu Leu Gln Ala Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu 90
 95 100
 15 GAC ACT CTG CAG CTA GAT GTA GCT GAC TTT GCT ACT ACT ATT TGG CAA 389
 Asp Thr Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln 105
 110 115 120
 CAG ATG GAA GAG CTC GGT ATG GCA CCA GCT CTG CAA CCG ACT CAA GGT 437
 Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly 125
 130 135
 20 GCT ATG CCG GCA TTC GCT TCT GCA TTC CAG CGT CGT GCA GGA GGT GTA 485
 Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val 140
 145 150
 25 CTG GTT GCT TCT CAT CTG CAA TCT TTC CTG GAA GTA TCT TAC CGT GTT 533
 Leu Val Ala Ser His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val 155
 160 165
 CTG CGT CAT CTG GCT CAG CCG TAATAGAATT C 565
 Leu Arg His Leu Ala Gln Pro 170
 175

(2) INFORMATION FOR SEQ ID NO:2:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 175 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu 1
 5 10 15
 Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu 20
 25 30
 45 Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu 35
 40 45

Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
50 55 60
Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
65 70 75 80
Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
85 90 95
Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
100 105 110
Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
115 120 125
Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
130 135 140
Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145 150 155 160
Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
165 170 175

(2) INFORMATION FOR SEQ ID NO:3:

- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

CTTTCGCTG CGTGTCTGG AACAA

24

(2) INFORMATION FOR SEQ ID NO:4:

- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 23 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

ACAGGTCGT CGTATCCAGG GTG

23

(2) INFORMATION FOR SEQ ID NO:5:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 23 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

CACTGCAAGA ACGTCTGTGC GCT

23

(2) INFORMATION FOR SEQ ID NO:6:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 23 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

CGCTACTTAC CGTCTGTGCC ATC

23

(2) INFORMATION FOR SEQ ID NO:7:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 24 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

CTTTCTGCTG CGTTGTCTGG AACA

24

(2) INFORMATION FOR SEQ ID NO:8:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 23 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:
ACAGGTTGCT CGTATCCAGG GTG 23

5 (2) INFORMATION FOR SEQ ID NO:9:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 23 base pairs
(B) TYPE: nucleic acid
10 (C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: DNA
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:9:
15 CACTGCAAGA ACCTCTGTGC GCT 23

(2) INFORMATION FOR SEQ ID NO:10:
(i) SEQUENCE CHARACTERISTICS:
20 (A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: DNA
25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:10:
CTTTCTGCTG CGTGTCTGG AACA 24

30 (2) INFORMATION FOR SEQ ID NO:11:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 23 base pairs
(B) TYPE: nucleic acid
35 (C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: DNA
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:11:
40 ACAGGTTGCT CGTATCCAGG GTG 23

(2) INFORMATION FOR SEQ ID NO:12:
(i) SEQUENCE CHARACTERISTICS:
45 (A) LENGTH: 23 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single

50
65

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:12:

5 CGCTACTTAC CGTCTGTCCC ATC 23

(2) INFORMATION FOR SEQ ID NO:13:

10 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 24 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

15 (ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:13:

CTTTCTGCTG CGTGTCTGG AACA 24

(2) INFORMATION FOR SEQ ID NO:14:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 23 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

25 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:14:

30 CACTGCAAGA ACGTCTGTGC GCT 23

(2) INFORMATION FOR SEQ ID NO:15:

(i) SEQUENCE CHARACTERISTICS:

35 (A) LENGTH: 23 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:15:

CGCTACTTAC CGTCTGTGCC ATC 23

45

50

55

(2) INFORMATION FOR SEQ ID NO:16:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 23 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:16:

ACAGGTTTCGT CGTATCCAGG GTG

23

(2) INFORMATION FOR SEQ ID NO:17:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 23 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:17:

CACTGCAAGA ACGTCTGTGC GCT

23

(2) INFORMATION FOR SEQ ID NO:18:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 23 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:18:

CGCTACTTAC CGTCTGTGCC ATC

23

(2) INFORMATION FOR SEQ ID NO:19:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 24 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:19:
 CTTTCTGCTG CGTTGTCTGG AACA 24

5 (2) INFORMATION FOR SEQ ID NO:20:
 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 23 base pairs
 (B) TYPE: nucleic acid
 10 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
 (ii) MOLECULE TYPE: DNA
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:20:
 15 ACAGGTTGCT CGTATCCAGG GTG 23

(2) INFORMATION FOR SEQ ID NO:21:
 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 23 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
 20 (ii) MOLECULE TYPE: DNA
 25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:21:
 CACTGCAAGA ACGTCTGTGC GCT 23

30 (2) INFORMATION FOR SEQ ID NO:22:
 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 23 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 35 (D) TOPOLOGY: linear
 (ii) MOLECULE TYPE: DNA
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:22:
 40 CGCTACTTAC CGTCTGTGCC ATC 23

(2) INFORMATION FOR SEQ ID NO:23:
 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 23 base pairs
 45 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single

50

55

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:23:

TCTGCTGAAA GCTCTGGAAC AGG 23

(2) INFORMATION FOR SEQ ID NO:24:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 23 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

10 (ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:24:

CTTGTCATC TGAAGCTCTT CAG 23

(2) INFORMATION FOR SEQ ID NO:25:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 37 base pairs

(B) TYPE: nucleic acid

15 (C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:25:

20 GAAAAACTGT CGGCTACTTA CAACTGTCC CATCCGG 37

(2) INFORMATION FOR SEQ ID NO:26:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 22 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

25 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:26:

30 TTCGTAAAAAT CGCGGGTGAC GG 22

45

50

55

(2) INFORMATION FOR SEQ ID NO:27:

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 22 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:27:

TCATCTGGCT GCGCCGTAAT AG

22

(2) INFORMATION FOR SEQ ID NO:28:

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 22 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:28:

CCGTGTTCTG GCTCATCTGG CT

22

(2) INFORMATION FOR SEQ ID NO:29:

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 24 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:29:

GAAGTATCTT ACGCTGTTCT GGGT

24

(2) INFORMATION FOR SEQ ID NO:30:

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 25 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:30:
GAAGTATCTT ACTAAGTCTT GCGTC 25

5 (2) INFORMATION FOR SEQ ID NO:31:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 base pairs
(B) TYPE: nucleic acid
10 (C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: DNA
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:31:
15 CGCTACTTAC GCCTGTGCC AT 22

(2) INFORMATION FOR SEQ ID NO:32:
(i) SEQUENCE CHARACTERISTICS:
20 (A) LENGTH: 22 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: DNA
25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:32:
CAAACGTGTC AAGCCGAAG AG 22

30 (2) INFORMATION FOR SEQ ID NO:33:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 base pairs
(B) TYPE: nucleic acid
35 (C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: DNA
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:33:
40 CATCCGAAG CACTGGTACT GC 22

(2) INFORMATION FOR SEQ ID NO:34:
(i) SEQUENCE CHARACTERISTICS:
45 (A) LENGTH: 23 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single

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(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

8 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:34:

GGAACAGGTT GCTAAAATCC AGG 23

(2) INFORMATION FOR SEQ ID NO:35:

10 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 25 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

15 (ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:35:

GAAACAGGTTG GTGCGATCCA GGGTG 25

(2) INFORMATION FOR SEQ ID NO:36:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 22 base pairs

(B) TYPE: nucleic acid

25 (C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:36:

30 GAAATGTC TG GCACAGGTTG GT 22

(2) INFORMATION FOR SEQ ID NO:37:

(i) SEQUENCE CHARACTERISTICS:

35 (A) LENGTH: 19 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:37:

TCCAGGGTGC CGGTGCTGC 19

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(2) INFORMATION FOR SEQ ID NO:38:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 23 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:38:

AAGAGCTCGG TGAGGCACCA GCT

23

(2) INFORMATION FOR SEQ ID NO:39:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 23 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:39:

CTCAAGGTGC TGAGCCGCA TTC

23

(2) INFORMATION FOR SEQ ID NO:40:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 20 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:40:

GAGCTCGTGC TGGCACCAGC

20

(2) INFORMATION FOR SEQ ID NO:41:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 21 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:41:
TCAAGGTGCT CTGCGGCAT T 21

5 (2) INFORMATION FOR SEQ ID NO:42:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 23 base pairs
(B) TYPE: nucleic acid
10 (C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: DNA
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:42:
15 TCTGCGCAA GCCTTCTGC TGA 23

(2) INFORMATION FOR SEQ ID NO:43:
(i) SEQUENCE CHARACTERISTICS:
20 (A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: DNA
25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:43:
CTTTCGTCTG GCATGTCTGG AACA 24

30 (2) INFORMATION FOR SEQ ID NO:44:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
35 (C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: DNA
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:44:
40 CTATTTCGCA AGCGATGGAA GAGC 24

(2) INFORMATION FOR SEQ ID NO:45:
(i) SEQUENCE CHARACTERISTICS:
45 (A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single

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(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:45:

5 CAGATGGAAG CGCTCGGTAT G 21

(2) INFORMATION FOR SEQ ID NO:46:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 20 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

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(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:46:

15 GAGCTCGGTC TGGCACCAGC 20

(2) INFORMATION FOR SEQ ID NO:47:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 21 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

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(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:47:

25 TCAAGGTGCT CTGCCGGCAT T 21

(2) INFORMATION FOR SEQ ID NO:48:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 22 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

30

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:48:

35 GAAATGTCTG GCACAGGTTT GT 22

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(2) INFORMATION FOR SEQ ID NO:49:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 19 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:49:

TTCCGGAGCG CACAGTTTG

19

(2) INFORMATION FOR SEQ ID NO:50:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 23 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:50:

CGAGAAGGCC TCGGGTGTC AAC

23

(2) INFORMATION FOR SEQ ID NO:51:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 22 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:51:

ATGCCAAATT GCAGTAGCAA AG

22

(2) INFORMATION FOR SEQ ID NO:52:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 24 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:52:
 5 ACAACGGTTT AACGTCATCG TTTC 24

(2) INFORMATION FOR SEQ ID NO:53:
 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 22 base pairs
 (B) TYPE: nucleic acid
 10 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
 (ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:53:
 15 ATCAGCTACT GCTAGTCGA GA 22

(2) INFORMATION FOR SEQ ID NO:54:
 20 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 23 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
 25 (ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:54:
 TCAGTCGATG ACGATCGACG TCT 23

(2) INFORMATION FOR SEQ ID NO:55:
 30 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 22 base pairs
 (B) TYPE: nucleic acid
 35 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
 (ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:55:
 40 TTACGAACCG CTTCAGACA TT 22

(2) INFORMATION FOR SEQ ID NO:56:
 45 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 25 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single

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(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:56:
TAAATGCTT GGCGAAGTC TGTA 25

(2) INFORMATION FOR SEQ ID NO:57:

10 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

15 (ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:57:
GTAGCAATG CAGCTACATC TA 22

(2) INFORMATION FOR SEQ ID NO:58:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 25 base pairs
(B) TYPE: nucleic acid
25 (C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:58:
30 CATCATCGTT TACGTGATG TAGAT 25

(2) INFORMATION FOR SEQ ID NO:59:

(i) SEQUENCE CHARACTERISTICS:
35 (A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:59:
CCAAGAGAAG CACCCAGCAG 20

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(2) INFORMATION FOR SEQ ID NO:60:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 22 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:60:

AGGGTTCTCT TCGTGGGTCG TC

22

(2) INFORMATION FOR SEQ ID NO:61:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:61:

CACTGGCCGT GATAATGAGC

20

(2) INFORMATION FOR SEQ ID NO:62:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 19 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:62:

CTAGGCCAGG CATTACTGG

19

(2) INFORMATION FOR SEQ ID NO:63:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 21 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:63:
 CCCTGGCGG TGACTAG C 21

5 (2) INFORMATION FOR SEQ ID NO:64:
 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 33 base pairs
 (B) TYPE: nucleic acid
 10 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
 (ii) MOLECULE TYPE: DNA
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:64:
 15 AGCAGAAAGC TTCCGGCAG AGAAGAAGCA GGA 33

(2) INFORMATION FOR SEQ ID NO:65:
 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 54 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
 25 (ii) MOLECULE TYPE: DNA
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:65:
 GCCGCAAAGC TTTCGCTGA AATGCTGGA AGAGGTCGT AAAATCCAGG GTGA 54

30 (2) INFORMATION FOR SEQ ID NO:66:
 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 59 base pairs
 (B) TYPE: nucleic acid
 35 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
 (ii) MOLECULE TYPE: DNA
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:66:
 40 CTGGAATGCA GAAGCAAATG CCGGCATAGC ACCTTCAGTC GGTGCAGAG CTGGTGCCA 59

(2) INFORMATION FOR SEQ ID NO:67:
 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 175 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

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(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:67:

5 Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
1 5 10 15

Arg Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
20 25 30

10 Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
35 40 45

Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
50 55 60

15 Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
65 70 75 80

20 Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
85 90 95

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
100 105 110

25 Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
115 120 125

Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
130 135 140

30 Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145 150 155 160

Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
165 170 175

(2) INFORMATION FOR SEQ ID NO:68:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 175 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:68:

45 Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
1 5 10 15

50 Lys Cys Leu Glu Gln Val Arg Arg Ile Gln Gly Asp Gly Ala Ala Leu
20 25 30

EP 0 612 846 A1

Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
35 40 45
Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
5 50 55 60
Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
65 70 75 80
Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
10 85 90 95
Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
100 105 110
Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
15 115 120 125
Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
130 135 140
Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
20 145 150 155 160
Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
165 170 175

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(2) INFORMATION FOR SEQ ID NO:69:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 175 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

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(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:69:

35

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
1 5 10 15

Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
20 25 30

40

Gln Glu Arg Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
35 40 45

Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
50 55 60

45

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
65 70 75 80

Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
85 90 95

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Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
 100 105 110
 5 Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
 115 120 125
 Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
 130 135 140
 10 Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
 145 150 155 160
 Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
 165 170 175

(2) INFORMATION FOR SEQ ID NO:70:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 175 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:70:

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
 1 5 10
 Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
 20 25 30
 Gln Glu Lys Leu Cys Ala Thr Tyr Arg Leu Cys His Pro Glu Glu Leu
 35 40 45
 Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
 50 55 60
 Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
 65 70 75 80
 Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
 85 90 95
 Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
 100 105 110
 Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
 115 120 125
 Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
 130 135 140
 50 Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
 145 150 155 160

Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
 165 170 175

(2) INFORMATION FOR SEQ ID NO:71:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 175 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:71:

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
 1 5 10 15
 Arg Cys Leu Glu Gln Val Arg Arg Ile Gln Gly Asp Gly Ala Ala Leu
 20 25 30
 Gln Glu Arg Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
 35 40 45
 Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
 50 55 60
 Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
 65 70 75 80
 Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
 85 90 95
 Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
 100 105 110
 Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
 115 120 125
 Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
 130 135 140
 Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
 145 150 155 160
 Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
 165 170 175

(2) INFORMATION FOR SEQ ID NO:72:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 175 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

* (xi) SEQUENCE DESCRIPTION: SEQ ID NO:72:

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
 1 5 10 15
 Arg Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
 20 25 30
 Gln Glu Arg Leu Cys Ala Thr Tyr Arg Leu Cys His Pro Glu Glu Leu
 35 40 45
 Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
 50 55 60
 Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
 65 70 75 80
 Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
 85 90 95
 Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
 100 105 110
 Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
 115 120 125
 Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
 130 135 140
 Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
 145 150 155 160
 Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
 165 170 175

(2) INFORMATION FOR SEQ ID NO:73:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 175 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:73:

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
 1 5 10 15
 Lys Cys Leu Glu Gln Val Arg Arg Ile Gln Gly Asp Gly Ala Ala Leu
 20 25 30
 Gln Glu Arg Leu Cys Ala Thr Tyr Arg Leu Cys His Pro Glu Glu Leu
 35 40 45

Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
 50 55 60
 Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
 65 70 75 80
 Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
 85 90 95
 Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
 100 105 110
 Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
 115 120 125
 Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
 130 135 140
 Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
 145 150 155 160
 Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
 165 170 175

(2) INFORMATION FOR SEQ ID NO:74:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 175 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:74:

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
 1 5 10 15
 Arg Cys Leu Glu Gln Val Arg Arg Ile Gln Gly Asp Gly Ala Ala Leu
 20 25 30
 Gln Glu Arg Leu Cys Ala Thr Tyr Arg Leu Cys His Pro Glu Glu Leu
 35 40 45
 Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
 50 55 60
 Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
 65 70 75 80
 Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
 85 90 95
 Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
 100 105 110

Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
115 120 125

5 Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
130 135 140

Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145 150 155 160

10 Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
165 170 175

(2) INFORMATION FOR SEQ ID NO:75:

15

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 175 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

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(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:75:

25

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
1 5 10 15

Arg Cys Leu Glu Gln Val Arg Arg Ile Gln Gly Asp Gly Ala Ala Leu
20 25 30

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Gln Glu Lys Leu Cys Ala Thr Tyr Arg Leu Cys His Pro Glu Glu Leu
35 40 45

Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
50 55 60

35

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
65 70 75 80

Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
85 90 95

40

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
100 105 110

Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
115 120 125

45

Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
130 135 140

Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145 150 155 160

50

Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
165 170 175

55

(2) INFORMATION FOR SEQ ID NO:76:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 175 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:76:

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
 1 5 10 15
 Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
 20 25 30
 Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
 35 40 45
 Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
 50 55 60
 Cys Pro Ser Glu Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
 65 70 75 80
 Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
 85 90 95
 Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
 100 105 110
 Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
 115 120 125
 Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
 130 135 140
 Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
 145 150 155 160
 Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
 165 170 175

(2) INFORMATION FOR SEQ ID NO:77:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 175 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:77:

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
 1 5 10 15
 Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
 20 25 30
 Gln Glu Lys Leu Ser Ala Thr Tyr Lys Leu Ser His Pro Glu Glu Leu
 35 40 45
 Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
 50 55 60
 Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
 65 70 75 80
 Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
 85 90 95
 Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
 100 105 110
 Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
 115 120 125
 Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
 130 135 140
 Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
 145 150 155 160
 Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
 165 170 175

(2) INFORMATION FOR SEQ ID NO:78:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 175 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:78:

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
 1 5 10 15
 Lys Cys Leu Glu Gln Val Arg Lys Ile Ala Gly Asp Gly Ala Ala Leu
 20 25 30
 Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
 35 40 45
 Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
 50 55 60

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
 65 70 75 80
 Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
 85 90 95
 Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
 100 105 110
 Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
 115 120 125
 Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
 130 135 140
 Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
 145 150 155 160
 Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
 165 170 175
 (2) INFORMATION FOR SEQ ID NO:79:
 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 175 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear
 (ii) MOLECULE TYPE: protein
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:79:
 Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
 1 5 10 15
 Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
 20 25 30
 Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
 35 40 45
 Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
 50 55 60
 Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
 65 70 75 80
 Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
 85 90 95
 Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
 100 105 110
 Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
 115 120 125

Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
130 135 140

5 Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145 150 155 160

Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Ala Pro
165 170 175

10

(2) INFORMATION FOR SEQ ID NO:80:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 175 amino acids
15 (B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:80:

20

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
1 5 10 15

25

Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
20 25 30

Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
35 40 45

30

Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
50 55 60

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
65 70 75 80

35

Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
85 90 95

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
100 105 110

40

Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
115 120 125

Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
130 135 140

45

Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145 150 155 160

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Phe Leu Glu Val Ser Tyr Arg Val Leu Ala His Leu Ala Gln Pro
165 170 175

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(2) INFORMATION FOR SEQ ID NO:81:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 175 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:81:

```

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
 1          5          10          15
Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
15          20          25          30
Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
          35          40          45
Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
20          50          55          60
Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
          65          70          75          80
Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
25          85          90          95
Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
          100          105          110
Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
30          115          120          125
Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
          130          135          140
Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145          150          155          160
Phe Leu Glu Val Ser Tyr Ala Val Leu Arg His Leu Ala Gln Pro
40          165          170          175

```

(2) INFORMATION FOR SEQ ID NO:82:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 174 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:82:

EP 0 612 846 A1

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
 1 5 10 15
 Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
 20 25 30
 Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
 35 40 45
 Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
 50 55 60
 Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
 65 70 75 80
 Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
 85 90 95
 Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
 100 105 110
 Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
 115 120 125
 Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
 130 135 140
 Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
 145 150 155 160
 Phe Leu Glu Val Ser Tyr Val Leu Arg His Leu Ala Gln Pro
 165 170 174

30

(2) INFORMATION FOR SEQ ID NO:83:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 175 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

35

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:83:

40

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
 1 5 10 15
 Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
 20 25 30
 Gln Glu Lys Leu Cys Ala Thr Tyr Ala Leu Cys His Pro Glu Glu Leu
 35 40 45
 Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
 50 55 60

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EP 0 612 846 A1

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
 65 70 75 80
 5 Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
 85 90 95
 Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
 100 105 110
 10 Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
 115 120 125
 Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
 130 135 140
 15 Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
 145 150 155 160
 Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
 165 170 175

(2) INFORMATION FOR SEQ ID NO:84:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 175 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:84:

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
 1 5 10 15
 Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
 20 25 30
 Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys Lys Pro Glu Glu Leu
 35 40 45
 Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
 50 55 60
 Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
 65 70 75 80
 45 Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
 85 90 95
 Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
 100 105 110
 50 Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
 115 120 125

Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
 130 135 140
 Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
 145 150 155 160
 Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
 165 170 175

(2) INFORMATION FOR SEQ ID NO:85:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 175 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:85:

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
 1 5 10 15
 Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
 20 25 30
 Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Ala Leu
 35 40 45
 Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
 50 55 60
 Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
 65 70 75 80
 Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
 85 90 95
 Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
 100 105 110
 Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
 115 120 125
 Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
 130 135 140
 Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
 145 150 155 160
 Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
 165 170 175

(2) INFORMATION FOR SEQ ID NO:86:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 175 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:86:

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
 1 5 10 15
 Lys Cys Leu Glu Gln Val Ala Lys Ile Gln Gly Asp Gly Ala Ala Leu
 20 25 30
 Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
 35 40 45
 Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
 50 55 60
 Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
 65 70 75 80
 Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
 85 90 95
 Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
 100 105 110
 Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
 115 120 125
 Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
 130 135 140
 Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
 145 150 155 160
 Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
 165 170 175

(2) INFORMATION FOR SEQ ID NO:87:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 175 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:87:

EP 0 612 846 A1

```

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
 1          5          10          15
5 Lys Cys Leu Glu Gln Val Arg Ala Ile Gln Gly Asp Gly Ala Ala Leu
          20          25          30
Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
          35          40          45
10 Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
   50          55          60
Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
 65          70          75          80
15 Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
   85          90          95
Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
100          105          110
20 Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
   115          120          125
Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
130          135          140
25 Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
   145          150          155          160
Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
165          170          175
30

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(2) INFORMATION FOR SEQ ID NO:88:

```

(i) SEQUENCE CHARACTERISTICS:
35 (A) LENGTH: 175 amino acids
   (B) TYPE: amino acid
   (D) TOPOLOGY: linear

```

(ii) MOLECULE TYPE: protein

```

40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:88:

```

```

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
 1          5          10          15
45 Lys Cys Leu Ala Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
          20          25          30
Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
          35          40          45
50 Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
   50          55          60

```

55

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Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
 65 70 75 80
 5 Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
 85 90 95
 Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
 100 105 110
 10 Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
 115 120 125
 Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
 130 135 140
 15 Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
 145 150 155 160
 Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
 165 170 175

(2) INFORMATION FOR SEQ ID NO:89:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 175 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:89:

30 Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
 1 5 10 15
 Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Ala Gly Ala Ala Leu
 20 25 30
 35 Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
 35 40 45
 40 Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
 50 55 60
 Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
 65 70 75 80
 45 Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
 85 90 95
 Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
 100 105 110
 50 Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
 115 120 125

Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
130 135 140

Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145 150 155 160

Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
165 170 175

(2) INFORMATION FOR SEQ ID NO:90:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 175 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:90:

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
1 5 10 15

Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
20 25 30

Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
35 40 45

Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
50 55 60

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
65 70 75 80

Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
85 90 95

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
100 105 110

Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Glu Ala
115 120 125

Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
130 135 140

Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145 150 155 160

Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
165 170 175

(2) INFORMATION FOR SEQ ID NO:91:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 175 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:91:

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
 1 5 10 15
 Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
 20 25 30
 Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
 35 40 45
 Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
 50 55 60
 Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
 65 70 75 80
 Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
 85 90 95
 Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
 100 105 110
 Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
 115 120 125
 Pro Ala Leu Gln Pro Thr Gln Gly Ala Glu Pro Ala Phe Ala Ser Ala
 130 135 140
 Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
 145 150 155 160
 Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
 165 170 175

(2) INFORMATION FOR SEQ ID NO:92:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 175 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:92:

EP 0 612 846 A1

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe L u Leu
 1 5 10 15
 Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
 20 25 30
 Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
 35 40 45
 Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
 50 55 60
 Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
 65 70 75 80
 Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
 85 90 95
 Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
 100 105 110
 Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Leu Ala
 115 120 125
 Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
 130 135 140
 Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
 145 150 155 160
 Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
 165 170 175

30

(2) INFORMATION FOR SEQ ID NO:93:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 175 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

35

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:93:

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
 1 5 10 15
 Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
 20 25 30
 Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
 35 40 45
 Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
 50 55 60

50

55

EP 0 612 846 A1

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
 65 70 75 80
 Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
 85 90 95
 Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
 100 105 110
 Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
 115 120 125
 Pro Ala Leu Gln Pro Thr Gln Gly Ala Leu Pro Ala Phe Ala Ser Ala
 130 135 140
 Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
 145 150 155 160
 Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
 165 170 175

20

(2) INFORMATION FOR SEQ ID NO:94:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 175 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

25

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:94:

30

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
 1 5 10 15

Lys Ala Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
 20 25 30

35

Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
 35 40 45

Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
 50 55 60

40

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
 65 70 75 80

Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
 85 90 95

45

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
 100 105 110

Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
 115 120 125

50

55

Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
 130 135 140
 Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
 145 150 155 160
 Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
 165 170 175

(2) INFORMATION FOR SEQ ID NO:95:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 175 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:95:

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Glu Ser Phe Leu Leu
 1 5 10 15
 Lys Cys Leu Glu Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
 20 25 30
 Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
 35 40 45
 Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
 50 55 60
 Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
 65 70 75 80
 Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
 85 90 95
 Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
 100 105 110
 Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
 115 120 125
 Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
 130 135 140
 Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
 145 150 155 160
 Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
 165 170 175

(2) INFORMATION FOR SEQ ID NO:96:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 175 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:96:

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Glu Ser Phe Leu Leu
1 5 10 15
Lys Cys Leu Glu Glu Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
20 25 30
Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
35 40 45
Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
50 55 60
Cys Pro Ser Glu Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
65 70 75 80
Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
85 90 95
Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
100 105 110
Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
115 120 125
Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
130 135 140
Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145 150 155 160
Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
165 170 175

(2) INFORMATION FOR SEQ ID NO:97:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 175 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:97:

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Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Gly Phe Leu Leu
  1      5      10      15
5  Lys Cys Leu Ala Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
      20      25      30
    Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
      35      40      45
10 Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
   50      55      60
    Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
      65      70      75      80
15 Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
      85      90      95
    Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
      100      105      110
20 Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
      115      120      125
    Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
      130      135      140
25 Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
      145      150      155      160
30 Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
      165      170      175

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(2) INFORMATION FOR SEQ ID NO:98:

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35 (i) SEQUENCE CHARACTERISTICS:
    (A) LENGTH: 175 amino acids
    (B) TYPE: amino acid
    (D) TOPOLOGY: linear

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40 (ii) MOLECULE TYPE: protein

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:98:

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Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
  1      5      10      15
45 Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
      20      25      30
    Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
      35      40      45
50

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Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
 50 55 60
 5 Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
 65 70 75 80
 Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
 85 90 95
 10 Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
 100 105 110
 Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Leu Ala
 115 120 125
 15 Pro Ala Leu Gln Pro Thr Gln Gly Ala Leu Pro Ala Phe Ala Ser Ala
 130 135 140
 Phe Gln Arg Arg Ala Gly Val Leu Val Ala Ser His Leu Gln Ser
 145 150 155 160
 20 Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
 165 170 175

(2) INFORMATION FOR SEQ ID NO:99:

25 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 175 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

30 (ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:99:

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ala Phe Leu Leu
 1 5 10 15
 35 Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
 20 25 30
 Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
 35 40 45
 40 Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
 50 55 60
 Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
 65 70 75 80
 Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
 85 90 95
 50 Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
 100 105 110

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Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
 115 120 125
 5 Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
 130 135 140
 Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
 145 150 155 160
 10 Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
 165 170 175

(2) INFORMATION FOR SEQ ID NO:100:

15 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 175 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

20 (ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:100:

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
 1 5 10 15
 25 Ala Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
 20 25 30
 Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
 30 35 40 45
 Val Leu Leu Gly His Ser Leu Gly Ile Pro-Trp Ala Pro Leu Ser Ser
 50 55 60
 Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
 35 65 70 75 80
 Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
 85 90 95
 40 Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
 100 105 110
 Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
 115 120 125
 45 Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
 130 135 140
 Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
 145 150 155 160
 50 Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
 165 170 175

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(2) INFORMATION FOR SEQ ID NO:101:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 175 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:101:

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
 1 5 10 15
 Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
 20 25 30
 Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
 35 40 45
 Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
 50 55 60
 Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
 65 70 75 80
 Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
 85 90 95
 Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
 100 105 110
 Asp Phe Ala Thr Thr Ile Trp Gln Ala Met Glu Glu Leu Gly Met Ala
 115 120 125
 Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
 130 135 140
 Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
 145 150 155 160
 Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
 165 170 175

(2) INFORMATION FOR SEQ ID NO:102:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 175 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:102:

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
 1 5 10 15
 5 Lys Cys Leu Glu Ala Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
 20 25 30
 Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
 35 40 45
 10 Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
 50 55 60
 Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
 65 70 75 80
 15 Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
 85 90 95
 Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Val Ala
 100 105 110
 20 Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
 115 120 125
 Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
 130 135 140
 25 Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
 145 150 155 160
 Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
 165 170 175
 30

(2) INFORMATION FOR SEQ ID NO:103:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 175 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:103:

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
 1 5 10 15
 45 Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
 20 25 30
 Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys Ala Pro Glu Glu Leu
 35 40 45
 50 Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
 50 55 60
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Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
65 70 75 80
Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
85 90 95
Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
100 105 110
Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
115 120 125
Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
130 135 140
Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145 150 155 160
Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
165 170 175

(2) INFORMATION FOR SEQ ID NO:104:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 175 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:104:

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
1 5 10 15
Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
20 25 30
Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
35 40 45
Val Leu Leu Gly Ala Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
50 55 60
Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
65 70 75 80
Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
85 90 95
Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
100 105 110
Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
115 120 125

Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
 130 135 140

5 Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
 145 150 155 160

Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
 165 170 175

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 (2) INFORMATION FOR SEQ ID NO:105:

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 175 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

15
 (ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:105:

20 Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
 1 5 10 15

Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
 25 20 25 30

Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
 35 40 45

30 Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
 50 55 60

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
 65 70 75 80

35 Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
 85 90 95

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Ala Val Ala
 100 105 110

40 Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
 115 120 125

Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
 130 135 140

45 Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
 145 150 155 160

Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
 165 170 175

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(2) INFORMATION FOR SEQ ID NO:106:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 175 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:106:

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
1 5 10 15
Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
20 25 30
Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
35 40 45
Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
50 55 60
Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
65 70 75 80
Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
85 90 95
Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
100 105 110
Ala Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
115 120 125
Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
130 135 140
Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145 150 155 160
Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
165 170 175

(2) INFORMATION FOR SEQ ID NO:107:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 175 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:107:

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Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
 1 5 10 15
 Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Leu
 20 25 30
 Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
 35 40 45
 Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
 50 55 60
 Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
 65 70 75 80
 Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
 85 90 95
 Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
 100 105 110
 Asp Phe Ala Thr Ala Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
 115 120 125
 Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
 130 135 140
 Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
 145 150 155 160
 Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
 165 170 175

(2) INFORMATION FOR SEQ ID NO:108:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 175 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:108:

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
 1 5 10 15
 Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Ala Gly Ala Leu
 20 25 30
 Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
 35 40 45
 Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
 50 55 60

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Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
 65 70 75 80
 5 Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
 85 90 95
 Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Ala Val Ala
 100 105 110
 10 Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
 115 120 125
 Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
 130 135 140
 15 Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
 145 150 155 160
 Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
 165 170 175
 20

(2) INFORMATION FOR SEQ ID NO:109:

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 175 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear
 25

(ii) MOLECULE TYPE: protein
 30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:109:

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
 1 5 10 15
 35 Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
 20 25 30
 Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
 35 40 45
 40 Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
 50 55 60
 Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
 65 70 75 80
 45 Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
 85 90 95
 Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
 100 105 110
 50

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Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Ala Leu Gly Met Ala
 115 120 125
 5 Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
 130 135 140
 Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
 145 150 155 160
 10 Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
 165 170 175

(2) INFORMATION FOR SEQ ID NO:110:

15 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 175 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

20 (ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:110:

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
 1 5 10 15
 25 Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
 20 25 30
 Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
 30 35 40 45
 Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
 50 55 60
 Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
 35 65 70 75 80
 Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
 85 90 95
 40 Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
 100 105 110
 Asp Val Ala Thr Ala Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
 115 120 125
 45 Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
 130 135 140
 Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
 145 150 155 160
 50 Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
 165 170 175

55 Claims

1. A method for preparing a G-CSF analog comprising the steps of:
 - (a) viewing information conveying the three dimensional structure of a G-CSF molecule;

- (b) selecting from said viewed information at least one site on said G-CSF molecule for alteration;
 - (c) preparing a G-CSF molecule having such alteration; and
 - (d) optionally, testing such G-CSF molecule for a desired characteristic.
- 5 2. A computer based method for preparing a G-CSF analog comprising the steps of:
- (a) providing computer expression of the three dimensional structure of a G-CSF molecule;
 - (b) selecting from said computer expression at least one site on said G-CSF molecule for alteration;
 - (c) preparing a G-CSF molecule having such alteration; and,
 - (d) optionally, testing such G-CSF molecule for a desired characteristic.
- 10 3. A method for preparing a G-CSF analog with the aid of a computer comprising:
- (a) providing said computer with the means for displaying the three dimensional structure of a G-CSF molecule including displaying the composition of moieties of said G-CSF molecule, preferably displaying the three dimensional location of each amino acid, and more preferably displaying the three dimensional location of each atom of a G-CSF molecule;
 - (b) viewing said display;
 - (c) selecting a site on said display for alteration in the composition of said molecule or the location of a moiety; and
 - (d) preparing a G-CSF analog with such alteration.
- 20 4. A computer-based method for preparing a G-CSF analog comprising the steps of:
- (a) viewing the three dimensional structure of a G-CSF molecule via a computer, said computer having been previously programmed (i) to express the coordinates of a G-CSF molecule in three dimensional space, and (ii) to allow for entry of information for alteration of said G-CSF expression and viewing thereof;
 - (b) selecting a site on said visual image of said G-CSF molecule for alteration;
 - (c) entering information for said alteration on said computer;
 - (d) viewing a three dimensional structure of said altered G-CSF molecule via said computer;
 - (e) optionally repeating steps (a)-(c) above;
 - (f) preparing a G-CSF analog with said alteration; and
 - (g) optionally testing said G-CSF analog for a desired characteristic.
- 30 5. In a computer-based apparatus for displaying the three dimensional structure of a molecule, the improvement comprising means for correlating said three dimensional structure of a G-CSF molecule with the composition of said G-CSF molecule.
- 35 6. A method for crystallization of a protein comprising the steps of:
- (a) combining, optionally by automated means, aqueous aliquots of said protein with either (i) aliquots of a salt solution, each aliquot having a different concentration of salt; or (ii) aliquots of a precipitant solution, each aliquot having a different concentration of precipitant;
 - (b) selecting at least one of said combined aliquots, said selection based on the formation of precrystalline forms, or, if no precrystalline forms are so produced, increasing the protein starting concentration of said aqueous aliquots of protein and repeating step (a);
 - (c) after said salt or said precipitant concentration is selected, repeating step (a) with said previously unselected solution in the presence of said selected concentration; and,
 - (d) repeating step (b) and step (a) until a crystal of desired quality is obtained.
- 45 7. A method of claim 6 wherein each combination pursuant to step (a) is performed in a range of pH.
- 50 8. A method of claim 6 wherein said combining of step (a) is done in the presence of a nucleation initiation unit.
9. A G-CSF analog having an amino acid sequence different from that of Figure 1 in that:
- (a) the N-terminal methionine is optional; and
 - (b) one or more of amino acids 58-72 (i) is substituted with one or more different amino acids or (ii) deleted; or (iii) chemically modified.
- 55

10. A G-CSF analog of claim 9 wherein said analog is more resistant to proteolysis than a G-CSF molecule of Figure 1.
11. A G-CSF analog of claim 10 wherein at least one of said amino acids is chemically modified by the addition of a polyethylene glycol molecule.
12. A G-CSF analog having an amino acid sequence different from that of Figure 1 in that:
 - (a) the N-terminal methionine is optional; and
 - (b) one or more of amino acids 119-125 (i) is substituted with one or more different amino acids or (ii) deleted; or (iii) chemically modified.
13. A G-CSF analog of claim 12 wherein said analog is more resistant to proteolysis than a G-CSF molecule of Figure 1.
14. A G-CSF analog of claim 12 wherein at least one of said amino acids is chemically modified by the addition of a polyethylene glycol molecule.
15. A G-CSF molecule having the AB loop stabilized by connecting such loop to one or more of helices A, B, C, or D.
16. A G-CSF molecule having the CD loop stabilized by connecting such loop to one or more of helices A, B, C, or D.
17. A G-CSF analog, optionally in a pharmaceutically effective carrier, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Lys¹⁷->Arg¹⁷ and the N-terminal methionine is optional.
18. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Lys³⁵->Arg³⁵ and the N-terminal methionine is optional.
19. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Lys⁴¹->Arg⁴¹ and the N-terminal methionine is optional.
20. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Lys^{17,24,35}->Arg^{17,24,35} and the N-terminal methionine is optional.
21. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Lys^{17,35,41}->Arg^{17,35,41} and the N-terminal methionine is optional.
22. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Lys^{24,35,41}->Arg^{24,35,41} and the N-terminal methionine is optional.
23. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Lys^{17,24,35,41}->Arg^{17,24,35,41} and the N-terminal methionine is optional.
24. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Lys^{17,24,41}->Arg^{17,24,41} and the N-terminal methionine is optional.
25. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Gln⁵¹->Glu⁵¹ and the N-terminal methionine is optional.
26. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Cys^{37,43}->Ser^{37,43} and the N-terminal methionine is optional.
27. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Gln²⁶->Ala²⁶ and the N-terminal methionine is optional.

28. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Gln¹⁷⁴->Ala¹⁷⁴ and the N-terminal methionine is optional.
29. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Arg¹⁷⁰->Ala¹⁷⁰ and the N-terminal methionine is optional.
30. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Arg¹⁶⁷->Ala¹⁶⁷ and the N-terminal methionine is optional.
31. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that there is a deletion at position 167 and the N-terminal methionine is optional.
32. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Lys¹⁴->Ala¹⁴ and the N-terminal methionine is optional.
33. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that His⁴⁴->Lys⁴⁴ and the N-terminal methionine is optional.
34. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Glu⁴⁷->Ala⁴⁷ and the N-terminal methionine is optional.
35. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Arg²³->Ala²³ and the N-terminal methionine is optional.
36. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Lys²⁴->Ala²⁴ and the N-terminal methionine is optional.
37. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Glu²⁰->Ala²⁰ and the N-terminal methionine is optional.
38. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Asp²⁸->Ala²⁸ and the N-terminal methionine is optional.
39. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Met²⁷->Glu²⁷ and the N-terminal methionine is optional.
40. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Met¹³⁸->Glu¹³⁸ and the N-terminal methionine is optional.
41. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Met¹²⁷->Leu¹²⁷ and the N-terminal methionine is optional.
42. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Met¹³⁸->Leu¹³⁸ and the N-terminal methionine is optional.
43. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Cys¹⁸->Ala¹⁸ and the N-terminal methionine is optional.
44. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Gln^{12,21}->Glu^{12,21} and the N-terminal methionine is optional.
45. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Gln^{12,21,68}->Glu^{12,21,68} and the N-terminal methionine is optional.
46. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Glu²⁰->Ala²⁰; Ser¹⁵->Gly¹³ and the N-terminal methionine is optional.

47. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Met^{127,128}->Leu^{127,128} and the N-terminal methionine is optional.
48. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Ser¹³->Ala¹³ and the N-terminal methionine is optional.
49. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Lys¹⁷->Ala¹⁷ and the N-terminal methionine is optional.
50. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Gln¹²¹->Ala¹²¹ and the N-terminal methionine is optional.
51. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Gln²¹->Ala²¹ and the N-terminal methionine is optional.
52. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that His⁴⁴->Ala⁴⁴ and the N-terminal methionine is optional.
53. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein said amino acid sequence differs from that of Figure 1 in that His⁵³->Ala⁵³ and the N-terminal methionine is optional.
54. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Asp¹¹⁰->Ala¹¹⁰ and the N-terminal methionine is optional.
55. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Asp¹¹³->Ala¹¹³ and the N-terminal methionine is optional.
56. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Thr¹¹⁷->Ala¹¹⁷ and the N-terminal methionine is optional.
57. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Asp²⁸->Ala²⁸; Asp¹¹⁰ ->Ala¹¹⁰ and the N-terminal methionine is optional.
58. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Glu¹²⁴->Ala¹²⁴ and the N-terminal methionine is optional.
59. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Phe¹¹⁴->Val¹¹⁴, Thr¹¹⁷->Ala¹¹⁷ and the N-terminal methionine is optional.
60. The G-CSF analog DNA-containing plasmids and bacterial host cells transformed therewith available from the American Type Culture Collection under the accession numbers ATCC 69184, 69185, 69186, 69187, 69188, 69189, 69190, 69191, 69192, 69193, 69194, 69195, 69196, 69197, 69198, 69199, 69200, 69201, 69202, 69203, 69204, 69205, 69206, 69207, 69208, 69209, 69210, 69211, 69212, 69213, 69214, 69215, 69216, 69217, 69218, 69219, 69220, 69221, 69222, 69223, 69224, 69225 and 69226.

Met Thr Pro Leu Gly Pro Ala
TCTAGAAAAAACCAGGAGGTAATAAATA ATG ACT CCA TTA GGT CCT CTT

Ser Ser Leu Pro Gln Ser Phe Leu Leu Lys Cys Leu Gln Gln
TCT TCT CTG CCG CAA AGC TTT CTG CTG AAA TGT CTG GAA CAG

Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys Leu
GTT CGT AAA ATC CAG GGT GAC GGT GCT GCA CTG CAA GAA AAA CTG

Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu Leu
TGC GCT ACT TAC AAA CTG TGC CAT CCG GAA GAG CTG GTA CTG CTG

Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro
GGT CAT TCT CTT GGG ATC CCG TGG GCT CCG CTG TCT TCT TGT CCA

Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser
TCT CAA GCT CTT CAG CTG GCT GGT TGT CTG TCT CAA CTG CAT TCT

Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
GGT CTG TTC CTG TAT CAG GGT CTT CTG CAA GCT CTG GAA GGT ATC

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val
TCT CCG GAA CTG GGT CCG ACT CTG GAC ACT CTG CAG CTA GAT GTA

Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly
GCT GAC TTT GCT ACT ACT ATT TGG CAA CAG ATG GAA GAG CTC GGT

Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe
ATG GCA CCA GCT CTG CAA CCG ACT CAA GGT GCT ATG CCG GCA TTC

Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser
GCT TCT GCA TTC CAG CGT CGT GCA GGA GGT GTA CTG GTT GCT TCT

His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His
CAT CTG CAA TCT TTC CTG GAA GTA TCT TAC CGT GTT CTG CGT CAT

Leu Ala Gln Pro OC AM
CTG GCT CAG CCG TAA TAG AATTC

FIGURE 1

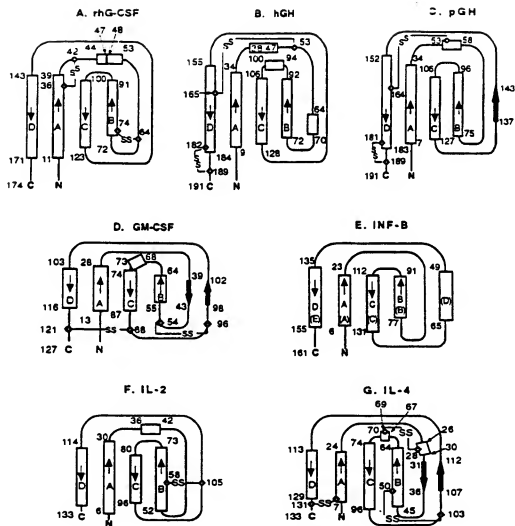


FIGURE 2

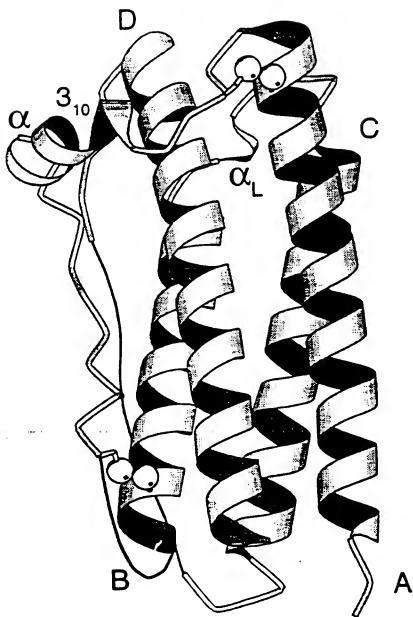


FIGURE 3

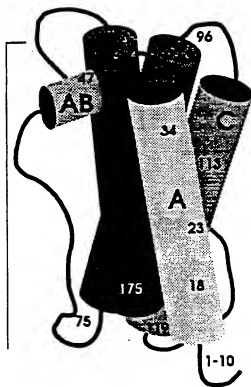


FIGURE 4

FIGURE 5

ATOM	1	CB	LEU	10	58.751	58.491	-14.865	1.00	61.12	A1
ATOM	2	CG	LEU	10	58.160	59.271	-15.589	1.00	61.12	A1
ATOM	3	CD	LEU	10	59.307	60.461	-14.023	1.00	60.618	A1
ATOM	4	CHI	LEU	10	56.954	56.628	-14.335	1.00	60.618	A1
ATOM	5	CHI	LEU	10	56.954	56.628	-14.335	1.00	60.618	A1
ATOM	6	O	LEU	10	60.079	55.595	-14.041	1.00	61.000	A1
ATOM	7	HTI	LEU	10	59.876	56.135	-15.998	1.00	0.000	A1
ATOM	8	HTI	LEU	10	61.221	56.887	-16.434	1.00	0.000	A1
ATOM	9	HTI	LEU	10	61.221	56.887	-16.434	1.00	0.000	A1
ATOM	10	HTI	LEU	10	59.817	57.535	-16.971	1.00	0.000	A1
ATOM	11	CA	LEU	10	60.183	57.738	-14.941	1.00	62.58	A1
ATOM	12	CD	PRO	11	61.327	56.962	-12.780	1.00	61.96	A1
ATOM	13	CD	PRO	11	61.327	56.962	-12.780	1.00	61.96	A1
ATOM	14	CA	PRO	11	61.832	55.889	-11.906	1.00	61.34	A1
ATOM	15	CA	PRO	11	62.915	56.547	-11.643	1.00	59.77	A1
ATOM	16	CD	PRO	11	62.915	56.547	-11.643	1.00	59.77	A1
ATOM	17	CD	PRO	11	60.075	55.224	-11.029	1.00	60.618	A1
ATOM	18	O	PRO	11	60.075	55.224	-11.029	1.00	60.618	A1
ATOM	19	N	GLN	12	59.468	53.171	-10.743	1.00	57.22	A1
ATOM	20	N	GLN	12	59.468	53.171	-10.743	1.00	57.22	A1
ATOM	21	CA	GLN	12	59.779	51.646	-10.970	1.00	59.77	A1
ATOM	22	CA	GLN	12	59.779	51.646	-10.970	1.00	59.77	A1
ATOM	23	CD	GLN	12	57.170	49.465	-11.970	1.00	65.82	A1
ATOM	24	CD	GLN	12	57.170	49.465	-11.970	1.00	65.82	A1
ATOM	25	O	GLN	12	57.170	49.465	-11.970	1.00	65.82	A1
ATOM	26	NEI	GLN	12	57.277	51.534	-12.541	1.00	63.02	A1
ATOM	27	NEI	GLN	12	57.277	51.534	-12.541	1.00	63.02	A1
ATOM	28	NEI	GLN	12	57.277	51.534	-12.541	1.00	63.02	A1
ATOM	29	C	GLN	12	59.336	53.347	-9.245	1.00	55.34	A1
ATOM	30	O	GLN	12	59.336	53.347	-9.245	1.00	55.34	A1
ATOM	31	O	GLN	12	60.473	53.879	-9.378	1.00	53.46	A1
ATOM	32	O	GLN	12	60.473	53.879	-9.378	1.00	53.46	A1
ATOM	33	CA	SER	13	60.335	53.974	-7.168	1.00	57.86	A1
ATOM	34	CB	SER	13	61.704	54.144	-6.626	1.00	57.24	A1
ATOM	35	CG	SER	13	61.704	54.144	-6.626	1.00	57.24	A1
ATOM	36	HC	SER	13	58.334	53.551	-7.307	1.00	56.64	A1
ATOM	37	HC	SER	13	58.334	53.551	-7.307	1.00	56.64	A1
ATOM	38	O	SER	13	58.509	55.144	-6.160	1.00	53.55	A1
ATOM	39	O	SER	13	58.509	55.144	-6.160	1.00	53.55	A1
ATOM	40	CA	PHE	14	59.791	56.333	-7.577	1.00	50.84	A1
ATOM	41	CA	PHE	14	59.791	56.333	-7.577	1.00	50.84	A1
ATOM	42	CB	PHE	14	59.807	57.590	-7.423	1.00	47.21	A1
ATOM	43	CB	PHE	14	59.811	58.590	-6.454	1.00	44.68	A1
ATOM	44	CD	PHE	14	58.023	59.594	-10.723	1.00	40.40	A1
ATOM	45	CD	PHE	14	58.264	60.673	-7.978	1.00	40.40	A1
ATOM	46	CD	PHE	14	57.114	60.518	-10.507	1.00	35.59	A1
ATOM	47	CD	PHE	14	57.114	60.518	-10.507	1.00	35.59	A1
ATOM	48	CD	PHE	14	56.751	61.515	-9.635	1.00	41.56	A1
ATOM	49	C	PHE	14	56.751	61.515	-9.635	1.00	41.56	A1
ATOM	50	O	PHE	14	56.750	57.588	-8.805	1.00	46.07	A1
ATOM	51	N	LEU	15	57.298	56.509	-8.718	1.00	41.44	A1
ATOM	52	N	LEU	15	57.298	56.509	-8.718	1.00	41.44	A1
ATOM	53	CA	LEU	15	55.904	56.163	-9.287	1.00	1.000	A1
ATOM	54	CA	LEU	15	55.858	55.482	-10.000	1.00	48.72	A1
ATOM	55	CG	LEU	15	54.853	56.031	-11.269	1.00	51.65	A1
ATOM	56	CG	LEU	15	54.853	56.031	-11.269	1.00	51.65	A1
ATOM	57	CHI	LEU	15	54.320	54.906	-12.204	1.00	51.27	A1
ATOM	58	C	LEU	15	55.169	55.410	-10.014	1.00	44.07	A1
ATOM	59	C	LEU	15	55.169	55.410	-10.014	1.00	44.07	A1
ATOM	60	N	LEU	15	53.945	55.867	-7.959	1.00	45.46	A1
ATOM	61	N	LEU	15	53.945	55.867	-7.959	1.00	45.46	A1
ATOM	62	CA	LEU	16	56.781	54.501	-7.251	1.00	1.000	A1
ATOM	63	CA	LEU	16	56.781	54.501	-7.251	1.00	1.000	A1
ATOM	64	CG	LEU	16	55.840	57.661	-5.791	1.00	41.14	A1
ATOM	65	CG	LEU	16	55.840	57.661	-5.791	1.00	41.14	A1
ATOM	66	CHI	LEU	16	56.889	50.367	-6.598	1.00	41.68	A1
ATOM	67	CHI	LEU	16	56.889	50.367	-6.598	1.00	41.68	A1
ATOM	68	O	LEU	16	54.413	51.088	-7.030	1.00	42.75	A1
ATOM	69	N	LEU	17	55.471	55.279	-7.023	1.00	41.47	A1
ATOM	70	N	LEU	17	55.471	55.279	-7.023	1.00	41.47	A1
ATOM	71	CA	LEU	17	56.951	56.784	-7.350	1.00	1.000	A1
ATOM	72	CA	LEU	17	56.951	56.784	-7.350	1.00	1.000	A1
ATOM	73	CG	LEU	17	56.951	56.784	-7.350	1.00	1.000	A1
ATOM	74	CG	LEU	17	56.951	56.784	-7.350	1.00	1.000	A1
ATOM	75	CG	LEU	17	56.951	56.784	-7.350	1.00	1.000	A1
ATOM	76	CG	LEU	17	56.951	56.784	-7.350	1.00	1.000	A1
ATOM	77	CG	LEU	17	56.951	56.784	-7.350	1.00	1.000	A1
ATOM	78	CG	LEU	17	56.951	56.784	-7.350	1.00	1.000	A1
ATOM	79	CG	LEU	17	56.951	56.784	-7.350	1.00	1.000	A1
ATOM	80	CG	LEU	17	56.951	56.784	-7.350	1.00	1.000	A1
ATOM	81	CG	LEU	17	56.951	56.784	-7.350	1.00	1.000	A1
ATOM	82	CG	LEU	17	56.951	56.784	-7.350	1.00	1.000	A1
ATOM	83	CG	LEU	17	56.951	56.784	-7.350	1.00	1.000	A1
ATOM	84	CG	LEU	17	56.951	56.784	-7.350	1.00	1.000	A1
ATOM	85	CG	LEU	17	56.951	56.784	-7.350	1.00	1.000	A1
ATOM	86	CG	LEU	17	56.951	56.784	-7.350	1.00	1.000	A1
ATOM	87	CG	LEU	17	56.951	56.784	-7.350	1.00	1.000	A1
ATOM	88	CG	LEU	17	56.951	56.784	-7.350	1.00	1.000	A1
ATOM	89	CG	LEU	17	56.951	56.784	-7.350	1.00	1.000	A1
ATOM	90	CG	LEU	17	56.951	56.784	-7.350	1.00	1.000	A1
ATOM	91	CG	LEU	17	56.951	56.784	-7.350	1.00	1.000	A1
ATOM	92	CG	LEU	17	56.951	56.784	-7.350	1.00	1.000	A1
ATOM	93	CG	LEU	17	56.951	56.784	-7.350	1.00	1.000	A1
ATOM	94	CG	LEU	17	56.951	56.784	-7.350	1.00	1.000	A1
ATOM	95	CG	LEU	17	56.951	56.784	-7.350	1.00	1.000	A1
ATOM	96	CG	LEU	17	56.951	56.784	-7.350	1.00	1.000	A1
ATOM	97	CG	LEU	17	56.951	56.784	-7.350	1.00	1.000	A1
ATOM	98	CG	LEU	17	56.951	56.784	-7.350	1.00	1.000	A1
ATOM	99	CG	LEU	17	56.951	56.784	-7.350	1.00	1.000	A1
ATOM	100	CA	GLU	20	50.750	55.710	-1.748	1.00	55.40	A1

FIGURE 5

ATOM 101	CE	GLU	20	53.053	55.334	-1.167	1.00	35.25	AI
ATOM 102	CE	GLU	20	53.508	55.304	0.260	1.00	41.21	AI
ATOM 103	CD	GLU	20	54.000	55.304	0.260	1.00	41.21	AI
ATOM 104	OBI	GLU	20	54.320	54.660	1.546	1.00	36.78	AI
ATOM 105	OBI	GLU	20	54.708	54.766	-0.576	1.00	31.57	AI
ATOM 106	OBI	GLU	20	49.230	57.117	-0.316	1.00	31.25	AI
ATOM 107	O	GLU	20	50.660	58.167	-0.044	1.00	31.33	AI
ATOM 108	N	GIN	21	51.270	58.004	-2.794	1.00	0.00	AI
ATOM 109	N	GIN	21	51.316	58.045	-2.740	1.00	31.37	AI
ATOM 110	N	GIN	21	51.316	60.485	-2.740	1.00	31.37	AI
ATOM 111	CG	GIN	21	53.622	61.460	-1.504	1.00	42.67	AI
ATOM 112	CG	GIN	21	53.622	61.460	-1.504	1.00	42.67	AI
ATOM 113	CG	GIN	21	53.622	61.460	-1.504	1.00	42.67	AI
ATOM 114	CG	GIN	21	53.622	61.460	-1.504	1.00	42.67	AI
ATOM 115	NEZ	GIN	21	54.256	61.448	2.678	1.00	42.33	AI
ATOM 116	NEZ	GIN	21	53.963	60.840	-3.384	1.00	0.00	AI
ATOM 117	NEZ	GIN	21	55.026	61.022	-2.730	1.00	0.00	AI
ATOM 118	NEZ	GIN	21	55.026	61.022	-2.730	1.00	0.00	AI
ATOM 119	O	GIN	21	48.027	60.421	-1.563	1.00	28.65	AI
ATOM 120	N	VAL	22	48.682	59.119	-3.321	1.00	25.85	AI
ATOM 121	N	VAL	22	48.682	59.119	-3.321	1.00	25.85	AI
ATOM 122	CA	VAL	22	47.508	58.814	-5.526	1.00	24.09	AI
ATOM 123	CB	VAL	22	47.508	58.814	-5.526	1.00	24.09	AI
ATOM 124	CG1	VAL	22	46.154	58.378	-6.096	1.00	19.97	AI
ATOM 125	CG1	VAL	22	46.154	58.378	-6.096	1.00	19.97	AI
ATOM 126	C	VAL	22	46.418	58.199	-3.728	1.00	25.65	AI
ATOM 127	O	VAL	22	45.438	59.190	-2.800	1.00	29.31	AI
ATOM 128	N	ARG	23	45.643	56.719	-3.058	1.00	23.93	AI
ATOM 129	N	ARG	23	45.643	56.719	-3.058	1.00	23.93	AI
ATOM 130	CA	ARG	23	45.667	56.593	-1.892	1.00	20.67	AI
ATOM 131	CB	ARG	23	46.104	55.135	-1.635	1.00	20.45	AI
ATOM 132	CG	ARG	23	45.695	54.446	-3.769	1.00	21.54	AI
ATOM 133	CD	ARG	23	45.095	54.446	-3.769	1.00	21.54	AI
ATOM 134	NE	ARG	23	45.076	53.437	-4.809	1.00	24.82	AI
ATOM 135	NE	ARG	23	45.076	53.437	-4.809	1.00	24.82	AI
ATOM 136	NE	ARG	23	45.076	53.437	-4.809	1.00	24.82	AI
ATOM 137	NH1	ARG	23	43.567	54.669	-4.006	1.00	29.31	AI
ATOM 138	NH11	ARG	23	43.567	54.669	-4.006	1.00	29.31	AI
ATOM 139	NH12	ARG	23	43.567	54.669	-4.006	1.00	29.31	AI
ATOM 140	NH13	ARG	23	43.567	54.669	-4.006	1.00	29.31	AI
ATOM 141	NH14	ARG	23	43.567	54.669	-4.006	1.00	29.31	AI
ATOM 142	NH15	ARG	23	43.567	54.669	-4.006	1.00	29.31	AI
ATOM 143	NH16	ARG	23	43.567	54.669	-4.006	1.00	29.31	AI
ATOM 144	O	ARG	23	44.936	51.802	-6.793	1.00	0.00	AI
ATOM 145	N	LEU	24	46.485	58.015	-0.118	1.00	22.67	AI
ATOM 146	N	LEU	24	46.485	58.015	-0.118	1.00	22.67	AI
ATOM 147	CA	LEU	24	47.391	59.579	-1.166	1.00	22.03	AI
ATOM 148	CB	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 149	CD	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 150	CE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 151	CE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 152	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 153	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 154	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 155	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 156	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 157	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 158	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 159	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 160	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 161	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 162	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 163	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 164	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 165	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 166	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 167	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 168	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 169	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 170	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 171	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 172	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 173	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 174	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 175	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 176	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 177	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 178	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 179	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 180	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 181	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 182	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 183	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 184	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 185	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 186	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 187	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 188	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 189	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 190	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 191	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 192	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 193	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 194	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 195	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 196	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 197	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 198	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 199	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 200	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 201	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 202	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 203	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 204	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 205	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 206	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 207	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 208	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 209	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 210	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 211	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 212	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 213	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 214	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 215	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 216	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 217	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 218	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 219	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 220	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 221	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 222	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 223	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 224	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 225	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 226	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 227	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 228	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 229	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 230	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 231	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 232	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 233	NE	LEU	24	47.811	59.555	-1.506	1.00	26.86	AI
ATOM 234	NE	LEU	24	47.811	59.555	-1.506	1.00		

FIGURE 5

ATOM 203 O ALA 30	37.149	50.772	3.754	1.00	28.42	A1
ATOM 204 N ALA 31	37.140	66.105	4.150	1.00	27.16	A1
ATOM 205 H ALA 31	38.751	60.114	3.809	1.00	0.00	A1
ATOM 206 C ALA 31	38.751	60.114	3.809	1.00	0.00	A1
ATOM 207 C β ALA 31	38.181	60.881	6.177	1.00	72.65	A1
ATOM 208 C ALA 31	36.178	61.675	5.660	1.00	80.01	A1
ATOM 209 O ALA 31	35.195	61.624	6.413	1.00	31.91	A1
ATOM 210 N LEU 32	37.133	62.734	4.242	1.00	0.00	A1
ATOM 211 H LEU 32	37.133	62.734	4.242	1.00	0.00	A1
ATOM 212 CA LEU 32	35.560	63.898	4.997	1.00	28.32	A1
ATOM 213 C α LEU 32	35.560	63.898	4.997	1.00	28.32	A1
ATOM 214 CG LEU 32	35.458	64.572	4.991	1.00	32.54	A1
ATOM 215 CD LEU 32	35.516	67.082	5.999	1.00	31.87	A1
ATOM 216 C β LEU 32	34.555	67.082	3.181	1.00	30.97	A1
ATOM 217 N GLN 33	33.977	63.028	3.315	1.00	77.51	A1
ATOM 218 O GLN 33	33.977	63.028	3.315	1.00	77.51	A1
ATOM 219 N GLN 33	33.977	63.028	3.315	1.00	77.51	A1
ATOM 220 C GLN 33	32.475	62.734	4.242	1.00	0.00	A1
ATOM 221 CA GLN 33	32.475	62.734	4.242	1.00	0.00	A1
ATOM 222 C α GLN 33	32.475	62.734	4.242	1.00	0.00	A1
ATOM 223 CG GLN 33	32.475	62.734	4.242	1.00	0.00	A1
ATOM 224 CD GLN 33	32.475	62.734	4.242	1.00	0.00	A1
ATOM 225 C β GLN 33	34.064	61.495	1.453	1.00	29.61	A1
ATOM 226 NE2 GLN 33	31.151	61.755	1.426	1.00	31.41	A1
ATOM 227 N THR 39	31.151	61.755	1.426	1.00	31.41	A1
ATOM 228 H2 α THR 39	31.151	61.755	1.426	1.00	31.41	A1
ATOM 229 C α THR 39	31.151	61.755	1.426	1.00	31.41	A1
ATOM 230 C β THR 39	31.151	61.755	1.426	1.00	31.41	A1
ATOM 231 H β THR 39	31.151	61.755	1.426	1.00	31.41	A1
ATOM 232 N GLU 34	33.140	66.707	4.318	1.00	0.00	A1
ATOM 233 C GLU 34	33.140	66.707	4.318	1.00	0.00	A1
ATOM 234 C α GLU 34	33.140	66.707	4.318	1.00	0.00	A1
ATOM 235 CG GLU 34	33.274	58.721	6.624	1.00	35.01	A1
ATOM 236 CD GLU 34	33.274	58.721	6.624	1.00	35.01	A1
ATOM 237 C β GLU 34	33.274	58.721	6.624	1.00	35.01	A1
ATOM 238 C γ GLU 34	33.274	58.721	6.624	1.00	35.01	A1
ATOM 239 C GLU 34	31.218	66.877	6.364	1.00	41.59	A1
ATOM 240 O GLU 34	30.175	66.877	7.161	1.00	44.87	A1
ATOM 241 N LYS 35	32.723	61.931	5.569	1.00	0.00	A1
ATOM 242 C LYS 35	32.723	61.931	5.569	1.00	0.00	A1
ATOM 243 CA LYS 35	31.674	62.634	8.134	1.00	45.43	A1
ATOM 244 C α LYS 35	31.674	62.634	8.134	1.00	45.43	A1
ATOM 245 CG LYS 35	33.701	62.414	9.510	1.00	32.75	A1
ATOM 246 CD LYS 35	35.084	62.021	9.548	1.00	57.55	A1
ATOM 247 C β LYS 35	36.067	62.099	10.218	1.00	60.35	A1
ATOM 248 H2 α LYS 35	34.631	61.723	11.640	1.00	0.00	A1
ATOM 249 H2 β LYS 35	33.910	61.011	12.078	1.00	0.00	A1
ATOM 250 H2 γ LYS 35	33.910	61.011	12.078	1.00	0.00	A1
ATOM 251 C LYS 35	30.810	63.660	1.697	1.00	44.45	A1
ATOM 252 O LYS 35	29.710	63.999	4.478	1.00	44.61	A1
ATOM 253 O LYS 35	29.710	63.999	4.478	1.00	44.61	A1
ATOM 254 N LEU 36	30.653	64.100	6.400	1.00	47.11	A1
ATOM 255 H LEU 36	31.143	63.140	5.806	1.00	47.00	A1
ATOM 256 CA LEU 36	29.647	63.157	6.144	1.00	46.75	A1
ATOM 257 C LEU 36	30.070	62.899	4.889	1.00	46.01	A1
ATOM 258 C α LEU 36	31.418	62.404	3.371	1.00	42.08	A1
ATOM 259 CH1 LEU 36	31.014	62.789	5.028	1.00	45.05	A1
ATOM 260 CH2 LEU 36	31.014	62.789	5.028	1.00	45.05	A1
ATOM 261 N LEU 36	27.252	64.474	5.941	1.00	41.96	A1
ATOM 262 O LEU 36	27.252	64.474	5.941	1.00	41.96	A1
ATOM 263 C LEU 36	27.252	64.474	5.941	1.00	41.96	A1
ATOM 264 H β LEU 36	27.252	64.474	5.941	1.00	41.96	A1
ATOM 265 C α LEU 36	27.252	64.474	5.941	1.00	41.96	A1
ATOM 266 C β LEU 36	27.252	64.474	5.941	1.00	41.96	A1
ATOM 267 O CYS 37	25.016	61.997	6.459	1.00	46.46	A1
ATOM 268 C CYS 37	25.016	61.997	6.459	1.00	46.46	A1
ATOM 269 C α CYS 37	25.016	61.997	6.459	1.00	46.46	A1
ATOM 270 N ALA 38	27.458	63.780	8.770	1.00	0.00	A1
ATOM 271 H ALA 38	27.458	63.780	8.770	1.00	0.00	A1
ATOM 272 CA ALA 38	27.458	63.780	8.770	1.00	0.00	A1
ATOM 273 C α ALA 38	27.458	63.780	8.770	1.00	0.00	A1
ATOM 274 C ALA 38	27.458	63.780	8.770	1.00	0.00	A1
ATOM 275 H THR 39	27.458	63.780	8.770	1.00	0.00	A1
ATOM 276 N THR 39	27.458	63.780	8.770	1.00	0.00	A1
ATOM 277 H THR 39	27.458	63.780	8.770	1.00	0.00	A1
ATOM 278 C α THR 39	27.458	63.780	8.770	1.00	0.00	A1
ATOM 279 C β THR 39	27.458	63.780	8.770	1.00	0.00	A1
ATOM 280 C γ THR 39	27.458	63.780	8.770	1.00	0.00	A1
ATOM 281 H β THR 39	27.458	63.780	8.770	1.00	0.00	A1
ATOM 282 H γ THR 39	27.458	63.780	8.770	1.00	0.00	A1
ATOM 283 C THR 39	25.775	65.465	10.037	1.00	52.17	A1
ATOM 284 O THR 39	24.886	65.882	10.781	1.00	52.17	A1
ATOM 285 H THR 40	26.420	65.331	8.139	1.00	0.00	A1
ATOM 286 H THR 40	26.420	65.331	8.139	1.00	0.00	A1
ATOM 287 CA THR 40	24.719	66.561	8.163	1.00	52.55	A1
ATOM 288 C THR 40	24.719	66.561	8.163	1.00	52.55	A1
ATOM 289 CG THR 40	24.719	66.561	8.163	1.00	52.55	A1
ATOM 290 CD THR 40	24.719	66.561	8.163	1.00	52.55	A1
ATOM 291 CE1 THR 40	24.719	66.561	8.163	1.00	52.55	A1
ATOM 292 CE2 THR 40	24.719	66.561	8.163	1.00	52.55	A1
ATOM 293 CE3 THR 40	24.719	66.561	8.163	1.00	52.55	A1
ATOM 294 C α THR 40	24.719	66.561	8.163	1.00	52.55	A1
ATOM 295 C β THR 40	24.719	66.561	8.163	1.00	52.55	A1
ATOM 296 H1 THR 40	24.719	66.561	8.163	1.00	52.55	A1
ATOM 297 C THR 40	24.035	65.911	6.981	1.00	51.75	A1
ATOM 298 O THR 40	23.662	66.578	6.074	1.00	52.52	A1
ATOM 299 H THR 40	24.474	64.064	7.583	1.00	0.00	A1
ATOM 300 H LYS 41	24.474	64.064	7.583	1.00	0.00	A1
ATOM 301 CA LYS 41	23.117	63.885	6.059	1.00	50.48	A1
ATOM 302 C LYS 41	23.117	63.885	6.059	1.00	50.48	A1
ATOM 303 CE1 LYS 41	21.387	63.136	7.911	1.00	53.11	A1
ATOM 304 CD LYS 41	20.112	63.878	8.574	1.00	55.54	A1

FIGURE 5

ATOM 305 C	115	41	19.378	63.087	9.820	1.00	48.79	AI	ATOM 336 C	GLU	46	22.181	65.334	-6.937	1.00	42.96	AI
ATOM 306 H	115	41	17.460	63.688	9.757	1.00	0.00	AI	ATOM 337 N	GLU	47	22.919	65.363	-5.654	1.00	41.96	AI
ATOM 307 H	115	41	18.578	64.607	10.803	1.00	0.00	AI	ATOM 338 N	GLU	47	23.507	65.098	-5.028	1.00	41.00	AI
ATOM 308 H	115	41	19.700	65.528	11.824	1.00	0.00	AI	ATOM 339 C	GLU	47	24.383	65.583	-5.965	1.00	41.72	AI
ATOM 309 H	115	41	21.823	66.349	12.743	1.00	0.00	AI	ATOM 340 C	GLU	47	21.794	65.421	-3.984	1.00	41.72	AI
ATOM 310 H	115	41	23.946	67.170	13.662	1.00	0.00	AI	ATOM 341 C	GLU	47	20.812	64.907	-1.547	1.00	47.86	AI
ATOM 311 N	LEU	42	24.437	64.893	4.346	1.00	48.28	AI	ATOM 342 C	GLU	47	20.812	64.907	-1.547	1.00	47.86	AI
ATOM 312 N	LEU	42	24.437	64.893	4.346	1.00	48.28	AI	ATOM 343 C	GLU	47	20.812	64.907	-1.547	1.00	47.86	AI
ATOM 313 H	LEU	42	24.437	64.893	4.346	1.00	48.28	AI	ATOM 344 C	GLU	47	20.812	64.907	-1.547	1.00	47.86	AI
ATOM 314 H	LEU	42	24.437	64.893	4.346	1.00	48.28	AI	ATOM 345 C	GLU	47	20.812	64.907	-1.547	1.00	47.86	AI
ATOM 315 C	LEU	42	25.565	66.574	2.757	1.00	46.61	AI	ATOM 346 C	GLU	47	22.795	67.718	-4.809	1.00	44.694	AI
ATOM 316 C	LEU	42	24.807	67.802	3.718	1.00	42.63	AI	ATOM 347 C	GLU	47	21.532	68.547	-4.792	1.00	44.694	AI
ATOM 317 C	LEU	42	24.807	67.802	3.718	1.00	42.63	AI	ATOM 348 C	GLU	47	24.160	67.310	-5.465	1.00	41.00	AI
ATOM 318 C	LEU	42	24.807	67.802	3.718	1.00	42.63	AI	ATOM 349 C	GLU	47	24.160	67.310	-5.465	1.00	41.00	AI
ATOM 319 C	LEU	42	24.807	67.802	3.718	1.00	42.63	AI	ATOM 350 C	GLU	47	24.160	67.310	-5.465	1.00	41.00	AI
ATOM 320 O	LEU	42	26.766	64.017	2.711	1.00	46.43	AI	ATOM 351 C	GLU	47	24.160	67.310	-5.465	1.00	41.00	AI
ATOM 321 O	LEU	42	26.766	64.017	2.711	1.00	46.43	AI	ATOM 352 C	GLU	47	24.160	67.310	-5.465	1.00	41.00	AI
ATOM 322 C	LEU	42	24.807	67.802	3.718	1.00	42.63	AI	ATOM 353 C	GLU	47	24.160	67.310	-5.465	1.00	41.00	AI
ATOM 323 C	LEU	42	24.807	67.802	3.718	1.00	42.63	AI	ATOM 354 C	GLU	47	24.160	67.310	-5.465	1.00	41.00	AI
ATOM 324 C	LEU	42	24.807	67.802	3.718	1.00	42.63	AI	ATOM 355 C	GLU	47	24.160	67.310	-5.465	1.00	41.00	AI
ATOM 325 C	LEU	42	24.807	67.802	3.718	1.00	42.63	AI	ATOM 356 C	GLU	47	24.160	67.310	-5.465	1.00	41.00	AI
ATOM 326 C	LEU	42	24.807	67.802	3.718	1.00	42.63	AI	ATOM 357 C	GLU	47	24.160	67.310	-5.465	1.00	41.00	AI
ATOM 327 C	LEU	42	24.807	67.802	3.718	1.00	42.63	AI	ATOM 358 C	GLU	47	24.160	67.310	-5.465	1.00	41.00	AI
ATOM 328 C	LEU	42	24.807	67.802	3.718	1.00	42.63	AI	ATOM 359 C	GLU	47	24.160	67.310	-5.465	1.00	41.00	AI
ATOM 329 C	LEU	42	24.807	67.802	3.718	1.00	42.63	AI	ATOM 360 C	GLU	47	24.160	67.310	-5.465	1.00	41.00	AI
ATOM 330 C	LEU	42	24.807	67.802	3.718	1.00	42.63	AI	ATOM 361 C	GLU	47	24.160	67.310	-5.465	1.00	41.00	AI
ATOM 331 C	LEU	42	24.807	67.802	3.718	1.00	42.63	AI	ATOM 362 C	GLU	47	24.160	67.310	-5.465	1.00	41.00	AI
ATOM 332 C	LEU	42	24.807	67.802	3.718	1.00	42.63	AI	ATOM 363 C	GLU	47	24.160	67.310	-5.465	1.00	41.00	AI
ATOM 333 C	LEU	42	24.807	67.802	3.718	1.00	42.63	AI	ATOM 364 C	GLU	47	24.160	67.310	-5.465	1.00	41.00	AI
ATOM 334 C	LEU	42	24.807	67.802	3.718	1.00	42.63	AI	ATOM 365 C	GLU	47	24.160	67.310	-5.465	1.00	41.00	AI
ATOM 335 C	LEU	42	24.807	67.802	3.718	1.00	42.63	AI	ATOM 366 C	GLU	47	24.160	67.310	-5.465	1.00	41.00	AI
ATOM 336 C	LEU	42	24.807	67.802	3.718	1.00	42.63	AI	ATOM 367 C	GLU	47	24.160	67.310	-5.465	1.00	41.00	AI
ATOM 337 C	LEU	42	24.807	67.802	3.718	1.00	42.63	AI	ATOM 368 C	GLU	47	24.160	67.310	-5.465	1.00	41.00	AI
ATOM 338 C	LEU	42	24.807	67.802	3.718	1.00	42.63	AI	ATOM 369 C	GLU	47	24.160	67.310	-5.465	1.00	41.00	AI
ATOM 339 C	LEU	42	24.807	67.802	3.718	1.00	42.63	AI	ATOM 370 C	LEU	48	24.160	67.310	-5.465	1.00	41.00	AI
ATOM 340 C	LEU	42	24.807	67.802	3.718	1.00	42.63	AI	ATOM 371 C	LEU	48	24.160	67.310	-5.465	1.00	41.00	AI
ATOM 341 N	PRO	45	26.710	63.978	-3.667	1.00	43.07	AI	ATOM 372 C	LEU	48	24.160	67.310	-5.465	1.00	41.00	AI
ATOM 342 C	PRO	45	27.715	62.995	-4.570	1.00	42.50	AI	ATOM 373 C	LEU	48	24.160	67.310	-5.465	1.00	41.00	AI
ATOM 343 C	PRO	45	28.720	62.012	-5.473	1.00	41.93	AI	ATOM 374 C	LEU	48	24.160	67.310	-5.465	1.00	41.00	AI
ATOM 344 C	PRO	45	28.720	62.012	-5.473	1.00	41.93	AI	ATOM 375 C	LEU	48	24.160	67.310	-5.465	1.00	41.00	AI
ATOM 345 C	PRO	45	28.720	62.012	-5.473	1.00	41.93	AI	ATOM 376 C	LEU	48	24.160	67.310	-5.465	1.00	41.00	AI
ATOM 346 C	PRO	45	28.720	62.012	-5.473	1.00	41.93	AI	ATOM 377 N	VAL	49	24.566	69.366	-7.347	1.00	41.52	AI
ATOM 347 C	PRO	45	28.720	62.012	-5.473	1.00	41.93	AI	ATOM 378 N	VAL	49	24.566	69.366	-7.347	1.00	41.52	AI
ATOM 348 N	GLU	46	25.464	63.501	-6.223	1.00	45.36	AI	ATOM 379 N	VAL	49	24.566	69.366	-7.347	1.00	41.52	AI
ATOM 349 N	GLU	46	25.464	63.501	-6.223	1.00	45.36	AI	ATOM 380 C	VAL	49	24.566	69.366	-7.347	1.00	41.52	AI
ATOM 350 C	GLU	46	24.482	63.460	-9.445	1.00	58.48	AI	ATOM 381 C	VAL	49	24.566	69.366	-7.347	1.00	41.52	AI
ATOM 351 C	GLU	46	24.482	63.460	-9.445	1.00	58.48	AI	ATOM 382 C	VAL	49	24.566	69.366	-7.347	1.00	41.52	AI
ATOM 352 C	GLU	46	24.482	63.460	-9.445	1.00	58.48	AI	ATOM 383 C	VAL	49	24.566	69.366	-7.347	1.00	41.52	AI
ATOM 353 C	GLU	46	24.482	63.460	-9.445	1.00	58.48	AI	ATOM 384 C	VAL	49	24.566	69.366	-7.347	1.00	41.52	AI
ATOM 354 C	GLU	46	24.482	63.460	-9.445	1.00	58.48	AI	ATOM 385 N	LEU	50	23.565	71.602	-8.530	1.00	46.16	AI
ATOM 355 H	LEU	46	22.795	63.555	-11.332	1.00	48.11	AI	ATOM 386 N	LEU	50	23.565	71.602	-8.530	1.00	46.16	AI

FIGURE 5

ATOM 407 O G1Y 57	38.853	74.364	-8.033	1.00	47.06	A1
ATOM 408 N H1S 53	37.047	74.107	-6.653	1.00	47.02	A1
ATOM 409 H H1S 53	36.868	73.654	-9.271	1.00	0.00	A1
ATOM 410 CA H1S 53	37.009	75.104	-10.761	1.00	47.23	A1
ATOM 411 CG H1S 53	36.854	75.104	-10.761	1.00	47.23	A1
ATOM 412 CG H1S 53	36.016	73.399	-12.460	1.00	44.60	A1
ATOM 413 CD2 H1S 53	35.112	72.774	-13.200	1.00	47.49	A1
ATOM 414 CD3 H1S 53	35.112	72.774	-13.200	1.00	47.49	A1
ATOM 415 HH1 H1S 53	36.016	73.399	-12.460	1.00	44.60	A1
ATOM 416 CE1 H1S 53	26.954	71.641	-13.346	1.00	46.90	A1
ATOM 417 CE2 H1S 53	27.622	71.399	-11.064	1.00	42.03	A1
ATOM 418 CE3 H1S 53	35.294	71.033	-14.239	1.00	0.22	A1
ATOM 419 C H1S 53	26.953	76.535	-10.536	1.00	47.72	A1
ATOM 420 O H1S 53	37.622	77.399	-11.064	1.00	42.03	A1
ATOM 421 CA H1S 53	37.622	77.399	-11.064	1.00	42.03	A1
ATOM 422 H H1S 53	35.673	76.218	-9.001	1.00	0.00	A1
ATOM 423 CA H1S 53	25.792	78.278	-9.177	1.00	46.92	A1
ATOM 424 CD H1S 53	24.376	78.181	-8.389	1.00	45.86	A1
ATOM 425 CD H1S 53	24.376	78.181	-8.389	1.00	45.86	A1
ATOM 426 H1S SER 54	23.465	76.677	-8.918	1.00	0.00	A1
ATOM 427 C SER 54	26.939	76.033	-8.549	1.00	47.92	A1
ATOM 428 O SER 54	27.618	77.322	-7.793	1.00	0.00	A1
ATOM 429 N H1S 55	37.618	77.322	-7.793	1.00	0.00	A1
ATOM 430 H H1S 55	37.618	77.322	-7.793	1.00	0.00	A1
ATOM 431 CA H1S 55	38.853	75.104	-10.761	1.00	47.23	A1
ATOM 432 CG H1S 55	38.853	75.104	-10.761	1.00	47.23	A1
ATOM 433 CG H1S 55	38.853	75.104	-10.761	1.00	47.23	A1
ATOM 434 CD1 H1S 55	38.853	75.104	-10.761	1.00	47.23	A1
ATOM 435 CD2 H1S 55	38.853	75.104	-10.761	1.00	47.23	A1
ATOM 436 C H1S 55	38.853	75.104	-10.761	1.00	47.23	A1
ATOM 437 O H1S 55	38.853	75.104	-10.761	1.00	47.23	A1
ATOM 438 H H1S 55	38.853	75.104	-10.761	1.00	47.23	A1
ATOM 439 N GLY 56	38.853	75.104	-10.761	1.00	47.23	A1
ATOM 440 CA GLY 56	38.853	75.104	-10.761	1.00	47.23	A1
ATOM 441 CG GLY 56	38.853	75.104	-10.761	1.00	47.23	A1
ATOM 442 CD GLY 56	38.853	75.104	-10.761	1.00	47.23	A1
ATOM 443 N H1S 57	37.618	77.322	-7.793	1.00	0.00	A1
ATOM 444 H H1S 57	37.618	77.322	-7.793	1.00	0.00	A1
ATOM 445 CA H1S 57	38.853	75.104	-10.761	1.00	47.23	A1
ATOM 446 CG H1S 57	38.853	75.104	-10.761	1.00	47.23	A1
ATOM 447 CD2 H1S 57	38.853	75.104	-10.761	1.00	47.23	A1
ATOM 448 CD3 H1S 57	38.853	75.104	-10.761	1.00	47.23	A1
ATOM 449 C H1S 57	38.853	75.104	-10.761	1.00	47.23	A1
ATOM 450 O H1S 57	38.853	75.104	-10.761	1.00	47.23	A1
ATOM 451 CA H1S 58	38.853	75.104	-10.761	1.00	47.23	A1
ATOM 452 CG H1S 58	38.853	75.104	-10.761	1.00	47.23	A1
ATOM 453 CD H1S 58	38.853	75.104	-10.761	1.00	47.23	A1
ATOM 454 CD2 H1S 58	38.853	75.104	-10.761	1.00	47.23	A1
ATOM 455 CD3 H1S 58	38.853	75.104	-10.761	1.00	47.23	A1
ATOM 456 C H1S 58	38.853	75.104	-10.761	1.00	47.23	A1
ATOM 457 O H1S 58	38.853	75.104	-10.761	1.00	47.23	A1
ATOM 458 O PRO 58	37.047	74.107	-6.653	1.00	47.02	A1
ATOM 459 N TRP 59	37.009	75.104	-10.761	1.00	47.23	A1
ATOM 460 H TRP 59	36.868	73.654	-9.271	1.00	0.00	A1
ATOM 461 CA TRP 59	37.254	73.951	-12.760	1.00	0.00	A1
ATOM 462 CG TRP 59	35.254	70.712	-10.889	1.00	46.37	A1
ATOM 463 CD TRP 59	35.254	70.712	-10.889	1.00	46.37	A1
ATOM 464 CD2 TRP 59	35.254	70.712	-10.889	1.00	46.37	A1
ATOM 465 CD3 TRP 59	35.254	70.712	-10.889	1.00	46.37	A1
ATOM 466 CE1 TRP 59	36.274	70.861	-8.538	1.00	44.00	A1
ATOM 467 CE2 TRP 59	33.972	70.794	-11.354	1.00	45.17	A1
ATOM 468 CE3 TRP 59	33.972	70.794	-11.354	1.00	45.17	A1
ATOM 469 HH1 TRP 59	33.972	70.794	-11.354	1.00	45.17	A1
ATOM 470 C21 TRP 59	33.972	70.794	-11.354	1.00	45.17	A1
ATOM 471 C22 TRP 59	33.972	70.794	-11.354	1.00	45.17	A1
ATOM 472 C23 TRP 59	33.972	70.794	-11.354	1.00	45.17	A1
ATOM 473 C TRP 59	33.972	70.794	-11.354	1.00	45.17	A1
ATOM 474 O TRP 59	33.972	70.794	-11.354	1.00	45.17	A1
ATOM 475 H ALA 60	38.853	75.104	-10.761	1.00	47.23	A1
ATOM 476 CA ALA 60	38.853	75.104	-10.761	1.00	47.23	A1
ATOM 477 CG ALA 60	38.853	75.104	-10.761	1.00	47.23	A1
ATOM 478 CD ALA 60	38.853	75.104	-10.761	1.00	47.23	A1
ATOM 479 CE ALA 60	38.853	75.104	-10.761	1.00	47.23	A1
ATOM 480 O ALA 60	38.853	75.104	-10.761	1.00	47.23	A1
ATOM 481 N PRO 61	41.635	70.745	-14.966	1.00	53.44	A1
ATOM 482 CA PRO 61	41.635	70.745	-14.966	1.00	53.44	A1
ATOM 483 CG PRO 61	41.635	70.745	-14.966	1.00	53.44	A1
ATOM 484 CD PRO 61	41.635	70.745	-14.966	1.00	53.44	A1
ATOM 485 CE PRO 61	41.635	70.745	-14.966	1.00	53.44	A1
ATOM 486 O PRO 61	41.635	70.745	-14.966	1.00	53.44	A1
ATOM 487 O PRO 61	41.635	70.745	-14.966	1.00	53.44	A1
ATOM 488 N LEU 62	43.040	67.271	-16.486	1.00	50.08	A1
ATOM 489 CA LEU 62	43.040	67.271	-16.486	1.00	50.08	A1
ATOM 490 CG LEU 62	43.040	67.271	-16.486	1.00	50.08	A1
ATOM 491 CD LEU 62	43.040	67.271	-16.486	1.00	50.08	A1
ATOM 492 CE LEU 62	43.040	67.271	-16.486	1.00	50.08	A1
ATOM 493 O LEU 62	43.040	67.271	-16.486	1.00	50.08	A1
ATOM 494 CD2 LEU 62	43.040	67.271	-16.486	1.00	50.08	A1
ATOM 495 CD3 LEU 62	43.040	67.271	-16.486	1.00	50.08	A1
ATOM 496 OT1 LEU 62	43.040	67.271	-16.486	1.00	50.08	A1
ATOM 497 OT2 LEU 62	43.040	67.271	-16.486	1.00	50.08	A1
ATOM 498 CG LEU 72	56.719	61.408	-17.913	1.00	63.44	A2
ATOM 499 CD1 LEU 72	56.719	61.408	-17.913	1.00	63.44	A2
ATOM 500 CD2 LEU 72	56.719	61.408	-17.913	1.00	63.44	A2
ATOM 501 CD3 LEU 72	56.719	61.408	-17.913	1.00	63.44	A2
ATOM 502 O LEU 72	56.719	61.408	-17.913	1.00	63.44	A2
ATOM 503 O LEU 72	56.719	61.408	-17.913	1.00	63.44	A2
ATOM 504 HT1 LEU 72	56.469	64.643	-21.261	1.00	0.00	A2
ATOM 505 HT2 LEU 72	56.469	64.643	-21.261	1.00	0.00	A2
ATOM 506 N LEU 72	55.795	63.783	-20.999	1.00	66.73	A2
ATOM 507 HT3 LEU 72	55.795	63.783	-20.999	1.00	66.73	A2
ATOM 508 CA LEU 72	56.064	62.714	-19.517	1.00	64.31	A2

FIGURE 5.

ATOM 300 N ALA 73	56.807	66.066	-17.086	1.00	64.54	A2
ATOM 310 H ALA 73	57.690	65.804	-19.432	1.00	0.00	A2
ATOM 321 C ALA 73	56.703	67.433	-18.613	1.00	62.53	A2
ATOM 311 N ALA 73	57.015	66.956	-19.056	1.00	64.01	A2
ATOM 313 C ALA 73	55.401	68.024	-18.535	1.00	60.537	A2
ATOM 314 O ALA 73	54.801	68.180	-17.456	1.00	59.42	A2
ATOM 315 H GLY 74	54.693	68.126	-19.091	1.00	59.32	A2
ATOM 316 H GLY 74	54.693	68.126	-19.091	1.00	59.32	A2
ATOM 317 CA GLY 74	53.336	68.718	-19.816	1.00	55.99	A2
ATOM 318 C GLY 74	53.327	68.114	-18.865	1.00	60.37	A2
ATOM 319 N GLY 74	53.327	68.114	-18.865	1.00	60.37	A2
ATOM 320 N CYS 75	51.945	66.520	-19.010	1.00	59.80	A2
ATOM 321 H CYS 75	51.660	66.538	-19.839	1.00	0.00	A2
ATOM 322 CA CYS 75	51.602	66.376	-18.078	1.00	60.617	A2
ATOM 323 C CYS 75	51.602	66.376	-18.078	1.00	60.617	A2
ATOM 324 H CYS 75	51.602	66.376	-18.078	1.00	60.617	A2
ATOM 325 C CYS 75	49.832	64.323	-20.096	1.00	73.47	A2
ATOM 326 N CYS 75	51.502	66.346	-16.642	1.00	56.73	A2
ATOM 327 H CYS 75	51.502	66.346	-16.642	1.00	56.73	A2
ATOM 328 N LEU 76	52.795	66.462	-16.296	1.00	53.93	A2
ATOM 329 H LEU 76	53.423	66.043	-17.137	1.00	0.00	A2
ATOM 330 CA LEU 76	53.235	66.551	-15.044	1.00	57.94	A2
ATOM 331 CG LEU 76	55.375	65.511	-14.090	1.00	49.02	A2
ATOM 332 CD LEU 76	54.832	63.740	-14.698	1.00	46.76	A2
ATOM 333 CE LEU 76	54.832	63.740	-14.698	1.00	46.76	A2
ATOM 334 C LEU 76	53.093	65.545	-14.423	1.00	53.65	A2
ATOM 335 O LEU 76	52.731	67.716	-13.244	1.00	53.50	A2
ATOM 336 N SER 77	53.327	64.381	-16.424	1.00	0.00	A2
ATOM 337 H SER 77	53.327	64.381	-16.424	1.00	0.00	A2
ATOM 338 CA SER 77	52.882	65.932	-14.943	1.00	54.93	A2
ATOM 339 C SER 77	54.425	70.352	-16.940	1.00	63.35	A2
ATOM 340 H SER 77	54.425	70.352	-16.940	1.00	63.35	A2
ATOM 341 HC SER 77	54.949	69.637	-16.315	1.00	0.00	A2
ATOM 342 C SER 77	51.382	70.172	-14.759	1.00	53.47	A2
ATOM 343 H SER 77	51.382	70.172	-14.759	1.00	53.47	A2
ATOM 344 N GLN 78	50.509	65.301	-15.515	1.00	51.82	A2
ATOM 345 H GLN 78	50.509	65.301	-15.515	1.00	51.82	A2
ATOM 346 CA GLN 78	49.074	65.919	-15.449	1.00	50.74	A2
ATOM 347 C GLN 78	47.420	65.784	-17.160	1.00	62.33	A2
ATOM 348 CG GLN 78	46.557	64.960	-11.071	1.00	61.33	A2
ATOM 349 CD GLN 78	46.557	64.960	-11.071	1.00	61.33	A2
ATOM 350 CE GLN 78	45.769	64.885	-17.800	1.00	61.17	A2
ATOM 351 NE GLN 78	44.973	69.327	-16.932	1.00	0.00	A2
ATOM 352 H21 GLN 78	44.973	69.327	-16.932	1.00	0.00	A2
ATOM 353 H21 GLN 78	44.973	69.327	-16.932	1.00	0.00	A2
ATOM 354 C GLN 78	48.591	69.065	-14.011	1.00	48.17	A2
ATOM 355 O GLN 78	47.691	69.618	-13.368	1.00	46.31	A2
ATOM 356 N GLN 79	49.326	67.988	-13.368	1.00	45.89	A2
ATOM 357 H GLN 79	49.326	67.988	-13.368	1.00	45.89	A2
ATOM 358 CA GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 359 C GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 360 CD GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 361 CE GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 362 NE GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 363 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 364 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 365 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 366 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 367 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 368 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 369 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 370 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 371 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 372 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 373 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 374 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 375 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 376 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 377 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 378 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 379 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 380 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 381 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 382 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 383 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 384 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 385 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 386 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 387 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 388 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 389 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 390 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 391 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 392 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 393 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 394 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 395 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 396 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 397 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 398 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 399 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 400 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 401 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 402 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 403 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 404 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 405 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 406 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 407 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 408 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 409 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 410 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 411 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 412 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 413 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 414 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 415 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 416 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 417 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 418 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 419 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 420 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 421 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 422 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 423 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 424 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 425 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 426 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 427 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 428 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 429 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 430 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 431 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 432 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 433 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 434 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 435 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 436 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 437 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 438 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 439 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 440 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 441 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 442 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 443 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 444 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 445 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 446 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 447 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 448 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 449 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 450 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 451 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 452 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 453 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 454 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 455 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 456 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 457 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 458 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 459 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 460 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2
ATOM 461 H21 GLN 79	48.919	67.559	-12.296	1.00	44.54	A2

FIGURE 5

ATOM	611	O	PIRE	84	45.600	74.249	-5.558	1.00	42.71	A2
ATOM	612	N	LEU	85	45.190	73.953	-7.674	1.00	38.64	A2
ATOM	613	N	LEU	85	45.555	73.337	-8.428	1.00	41.00	A2
ATOM	614	CA	LEU	85	42.794	72.332	-8.384	1.00	38.81	A2
ATOM	615	CG	LEU	85	42.975	70.771	-9.434	1.00	36.76	A2
ATOM	616	CG	LEU	85	41.673	74.003	-9.017	1.00	46.45	A2
ATOM	617	CD	LEU	85	41.702	75.784	-9.719	1.00	47.80	A2
ATOM	618	C	LEU	85	41.702	75.784	-9.719	1.00	47.80	A2
ATOM	619	CD	LEU	85	42.078	72.743	-5.386	1.00	38.76	A2
ATOM	620	O	LEU	85	42.498	74.569	-5.381	1.00	38.36	A2
ATOM	621	N	TYR	86	43.150	72.605	-6.198	1.00	37.92	A2
ATOM	622	CA	TYR	86	43.150	72.605	-6.198	1.00	37.92	A2
ATOM	623	CG	TYR	86	41.501	71.801	-5.057	1.00	37.15	A2
ATOM	624	CD	TYR	86	42.598	70.555	-5.102	1.00	36.73	A2
ATOM	625	CG	TYR	86	41.561	69.685	-5.081	1.00	33.66	A2
ATOM	626	CD	TYR	86	40.724	69.623	-5.666	1.00	32.63	A2
ATOM	627	CD	TYR	86	40.724	69.623	-5.666	1.00	32.63	A2
ATOM	628	CH	TYR	86	40.991	68.881	-4.780	1.00	30.09	A2
ATOM	629	CH	TYR	86	38.670	68.418	-4.751	1.00	28.18	A2
ATOM	630	O	TYR	86	38.670	68.418	-4.751	1.00	28.18	A2
ATOM	631	OH	TYR	86	42.173	72.469	-2.889	1.00	31.52	A2
ATOM	632	HN	TYR	86	44.347	72.655	-3.478	1.00	36.93	A2
ATOM	633	HN	TYR	86	43.044	72.463	-4.140	1.00	30.00	A2
ATOM	634	O	TYR	86	42.740	72.335	-3.391	1.00	31.00	A2
ATOM	635	N	GLY	87	46.110	73.664	-2.255	1.00	39.56	A2
ATOM	636	CA	GLY	87	46.110	73.664	-2.255	1.00	39.56	A2
ATOM	637	CG	GLY	87	42.126	72.993	-1.237	1.00	46.99	A2
ATOM	638	CD	GLY	87	48.844	72.601	-1.607	1.00	52.15	A2
ATOM	639	CD	GLY	87	48.844	72.601	-1.607	1.00	52.15	A2
ATOM	640	CD	GLY	87	49.446	71.608	-0.663	1.00	51.96	A2
ATOM	641	NEZ	GLY	87	49.055	71.937	0.184	1.00	50.00	A2
ATOM	642	NEZ	GLY	87	49.055	71.937	0.184	1.00	50.00	A2
ATOM	643	NE21	GLY	87	43.941	74.653	-2.013	1.00	34.36	A2
ATOM	644	C	GLY	87	43.941	74.653	-2.013	1.00	34.36	A2
ATOM	645	C	GLY	87	43.941	74.653	-2.013	1.00	34.36	A2
ATOM	646	O	GLY	87	43.414	74.990	-0.935	1.00	31.55	A2
ATOM	647	N	GLY	88	42.740	72.335	-3.391	1.00	31.00	A2
ATOM	648	N	GLY	88	42.740	72.335	-3.391	1.00	31.00	A2
ATOM	649	CA	GLY	88	42.948	76.546	-3.232	1.00	30.81	A2
ATOM	650	C	GLY	88	41.540	76.735	-2.731	1.00	30.47	A2
ATOM	651	N	LEU	89	40.802	75.817	-3.046	1.00	29.01	A2
ATOM	652	CA	LEU	89	41.220	75.817	-3.046	1.00	29.01	A2
ATOM	653	N	LEU	89	39.447	75.102	-3.099	1.00	27.60	A2
ATOM	654	CA	LEU	89	39.447	75.102	-3.099	1.00	27.60	A2
ATOM	655	CG	LEU	89	38.764	74.583	-5.340	1.00	29.53	A2
ATOM	656	CD	LEU	89	38.764	74.583	-5.340	1.00	29.53	A2
ATOM	657	CD	LEU	89	38.363	73.530	-4.364	1.00	24.13	A2
ATOM	658	CD	LEU	89	37.673	72.639	-3.710	1.00	28.87	A2
ATOM	659	CD	LEU	89	37.673	72.639	-3.710	1.00	28.87	A2
ATOM	660	O	LEU	89	40.437	75.012	-0.860	1.00	30.81	A2
ATOM	661	N	LEU	90	40.317	73.819	-1.094	1.00	32.59	A2
ATOM	662	CA	LEU	90	40.182	73.626	-1.643	1.00	30.86	A2
ATOM	663	CA	LEU	90	40.182	73.626	-1.643	1.00	30.86	A2
ATOM	664	CB	LEU	90	41.207	72.234	0.303	1.00	36.35	A2
ATOM	665	CG	LEU	90	42.975	70.771	-9.434	1.00	36.76	A2
ATOM	666	CG	LEU	90	39.993	70.099	0.279	1.00	40.54	A2
ATOM	667	CD	LEU	90	40.342	74.319	1.255	1.00	44.21	A2
ATOM	668	C	LEU	90	40.342	74.319	1.255	1.00	44.21	A2
ATOM	669	N	GLN	91	41.188	75.791	0.940	1.00	35.24	A2
ATOM	670	N	GLN	91	41.188	75.791	0.940	1.00	35.24	A2
ATOM	671	N	GLN	91	41.563	75.284	0.078	1.00	40.80	A2
ATOM	672	CA	GLN	91	41.397	76.373	1.883	1.00	37.40	A2
ATOM	673	CG	GLN	91	43.155	78.237	2.384	1.00	44.42	A2
ATOM	674	CG	GLN	91	43.155	78.237	2.384	1.00	44.42	A2
ATOM	675	CD	GLN	91	44.348	78.799	1.542	1.00	50.96	A2
ATOM	676	CD	GLN	91	44.348	78.799	1.542	1.00	50.96	A2
ATOM	677	NE21	GLN	91	45.108	80.331	0.741	1.00	40.00	A2
ATOM	678	NE21	GLN	91	45.108	80.331	0.741	1.00	40.00	A2
ATOM	679	NE21	GLN	91	45.108	80.331	0.741	1.00	40.00	A2
ATOM	680	O	GLN	91	39.718	77.500	3.196	1.00	36.21	A2
ATOM	681	N	ALA	92	39.456	77.570	0.943	1.00	36.63	A2
ATOM	682	N	ALA	92	39.456	77.570	0.943	1.00	36.63	A2
ATOM	683	CA	ALA	92	38.745	78.436	0.311	1.00	40.76	A2
ATOM	684	CA	ALA	92	38.745	78.436	0.311	1.00	40.76	A2
ATOM	685	CB	ALA	92	37.657	78.436	0.311	1.00	40.76	A2
ATOM	686	C	ALA	92	37.159	77.905	1.770	1.00	38.95	A2
ATOM	687	N	GLU	93	37.159	77.905	1.770	1.00	38.95	A2
ATOM	688	N	GLU	93	37.159	77.905	1.770	1.00	38.95	A2
ATOM	689	CA	LEU	93	37.855	76.040	1.759	1.00	40.90	A2
ATOM	690	CA	LEU	93	37.855	76.040	1.759	1.00	40.90	A2
ATOM	691	CG	LEU	93	36.111	76.018	2.932	1.00	46.90	A2
ATOM	692	CG	LEU	93	36.111	76.018	2.932	1.00	46.90	A2
ATOM	693	CD	LEU	93	35.725	73.992	1.378	1.00	33.55	A2
ATOM	694	CD	LEU	93	35.725	73.992	1.378	1.00	33.55	A2
ATOM	695	CD	LEU	93	36.159	72.583	1.178	1.00	33.26	A2
ATOM	696	CD	LEU	93	36.159	72.583	1.178	1.00	33.26	A2
ATOM	697	N	GLU	94	36.464	76.310	4.426	1.00	46.41	A2
ATOM	698	O	LEU	93	35.473	75.917	5.236	1.00	35.17	A2
ATOM	699	N	GLU	94	37.357	77.019	4.736	1.00	48.19	A2
ATOM	700	CA	GLU	94	37.357	77.019	4.736	1.00	48.19	A2
ATOM	701	CG	GLU	94	37.627	77.573	6.018	1.00	47.71	A2
ATOM	702	CG	GLU	94	36.931	78.947	6.105	1.00	47.18	A2
ATOM	703	CG	GLU	94	36.931	78.947	6.105	1.00	47.18	A2
ATOM	704	CG	GLU	94	37.418	81.053	4.462	1.00	46.36	A2
ATOM	705	CG	GLU	94	35.728	81.107	3.823	1.00	46.76	A2
ATOM	706	CD	GLU	94	36.331	82.054	5.721	1.00	46.64	A2
ATOM	707	N	GLY	95	36.624	77.172	8.167	1.00	45.70	A2
ATOM	708	N	GLY	95	36.624	77.172	8.167	1.00	45.70	A2
ATOM	709	N	GLY	95	37.641	75.410	7.001	1.00	44.64	A2
ATOM	710	C	GLY	95	38.024	75.192	6.137	1.00	40.00	A2
ATOM	711	O	GLY	95	36.162	73.612	8.061	1.00	42.24	A2
ATOM	712	N	LEU	96	36.028	72.596	8.730	1.00	40.02	A2
ATOM	713	N	LEU	96	35.100	74.121	7.218	1.00	42.62	A2

FIGURE 5

ATOM 713 H HE 96	35.357	74.944	6.841	1.00	0.00	A2
ATOM 714 CA ILE 96	33.560	71.692	7.312	1.00	42.12	A2
ATOM 715 CG ILE 96	32.748	71.768	6.789	1.00	45.79	A2
ATOM 716 CD ILE 96	34.091	72.537	5.734	1.00	35.35	A2
ATOM 717 CG ILE 96	34.051	70.743	4.738	1.00	35.64	A2
ATOM 718 CD ILE 96	33.220	74.716	6.841	1.00	46.59	A2
ATOM 719 HE ILE 96	33.220	74.716	6.841	1.00	46.59	A2
ATOM 720 N SER 97	33.467	73.154	9.780	1.00	46.84	A2
ATOM 721 C SER 97	34.443	72.553	9.706	1.00	0.00	A2
ATOM 722 H SER 97	34.443	72.553	9.706	1.00	0.00	A2
ATOM 723 CG SER 97	31.405	70.573	11.427	1.00	0.00	A2
ATOM 724 CA SER 97	31.405	70.573	11.427	1.00	0.00	A2
ATOM 725 CG SER 97	31.405	70.573	11.427	1.00	0.00	A2
ATOM 726 H SER 97	31.405	70.573	11.427	1.00	0.00	A2
ATOM 727 N SER 97	31.405	70.573	11.427	1.00	0.00	A2
ATOM 728 O SER 97	35.035	72.538	11.678	1.00	51.78	A2
ATOM 729 N PRO 98	34.063	73.474	13.348	1.00	52.12	A2
ATOM 730 CD PRO 98	34.063	73.474	13.348	1.00	52.12	A2
ATOM 731 CG PRO 98	35.095	72.538	11.678	1.00	51.90	A2
ATOM 732 CA PRO 98	35.095	72.538	11.678	1.00	51.90	A2
ATOM 733 CG PRO 98	33.777	74.737	15.182	1.00	55.48	A2
ATOM 734 CD PRO 98	33.777	74.737	15.182	1.00	55.48	A2
ATOM 735 O PRO 98	36.378	71.274	14.468	1.00	57.45	A2
ATOM 736 N GLU 99	34.509	70.971	14.714	1.00	58.21	A2
ATOM 737 H GLU 99	33.657	71.400	14.028	1.00	0.00	A2
ATOM 738 C GLU 99	33.657	71.400	14.028	1.00	0.00	A2
ATOM 739 CG GLU 99	31.111	69.104	14.504	1.00	63.10	A2
ATOM 740 CD GLU 99	31.111	69.104	14.504	1.00	63.10	A2
ATOM 741 CG GLU 99	31.076	66.318	13.962	1.00	76.95	A2
ATOM 742 CD GLU 99	31.076	66.318	13.962	1.00	76.95	A2
ATOM 743 OE1 GLU 99	31.295	67.182	13.153	1.00	77.99	A2
ATOM 744 C GLU 99	35.398	69.025	13.074	1.00	55.31	A2
ATOM 745 O GLU 99	36.251	68.270	13.210	1.00	55.39	A2
ATOM 746 N LEU 100	34.214	70.159	11.841	1.00	0.00	A2
ATOM 747 H LEU 100	35.577	69.032	10.678	1.00	44.08	A2
ATOM 748 CA LEU 100	35.577	69.032	10.678	1.00	44.08	A2
ATOM 749 CD LEU 100	33.851	67.242	10.677	1.00	47.48	A2
ATOM 750 CG LEU 100	33.544	68.337	9.674	1.00	45.39	A2
ATOM 751 CD LEU 100	33.207	68.975	9.458	1.00	46.40	A2
ATOM 752 CG LEU 100	33.207	68.975	9.458	1.00	46.40	A2
ATOM 753 O LEU 100	37.578	69.244	9.357	1.00	46.62	A2
ATOM 754 C LEU 100	37.441	70.505	11.277	1.00	45.40	A2
ATOM 755 N GLY 101	37.441	70.505	11.277	1.00	45.40	A2
ATOM 756 CG GLY 101	38.702	70.138	11.276	1.00	45.12	A2
ATOM 757 CA GLY 101	39.885	70.334	10.794	1.00	40.73	A2
ATOM 758 O GLY 101	40.475	70.402	9.710	1.00	40.69	A2
ATOM 759 C GLY 101	40.475	70.402	9.710	1.00	40.69	A2
ATOM 760 CD LEU 102	39.676	65.150	13.027	1.00	38.76	A2
ATOM 761 CA LEU 102	39.676	65.150	13.027	1.00	38.76	A2
ATOM 762 CA PRO 103	41.390	68.566	11.606	1.00	37.30	A2
ATOM 763 CH PRO 103	41.294	67.690	12.775	1.00	39.16	A2
ATOM 764 CG PRO 102	40.799	68.087	13.776	1.00	41.02	A2
ATOM 765 C PRO 102	41.364	67.795	10.331	1.00	47.15	A2
ATOM 766 O PRO 102	42.358	67.854	9.600	1.00	48.88	A2
ATOM 767 H THR 103	39.466	67.233	10.662	1.00	51.16	A2
ATOM 768 CA THR 103	40.051	66.386	8.843	1.00	54.61	A2
ATOM 769 CD THR 103	38.592	65.888	8.715	1.00	54.67	A2
ATOM 770 CG THR 103	38.592	65.888	8.715	1.00	54.67	A2
ATOM 771 HG1 THR 103	38.011	65.896	10.548	1.00	51.70	A2
ATOM 772 CG1 THR 103	38.312	64.896	7.594	1.00	41.70	A2
ATOM 773 CG2 THR 103	38.312	64.896	7.594	1.00	41.70	A2
ATOM 774 H THR 103	41.291	67.215	7.425	1.00	44.61	A2
ATOM 775 C THR 103	41.291	67.215	7.425	1.00	44.61	A2
ATOM 776 N LEU 104	40.054	68.498	2.519	1.00	0.00	A2
ATOM 777 H LEU 104	39.504	68.923	8.219	1.00	0.00	A2
ATOM 778 C LEU 104	39.504	68.923	8.219	1.00	0.00	A2
ATOM 779 CG LEU 104	39.616	70.430	6.242	1.00	31.49	A2
ATOM 780 CD LEU 104	38.356	68.996	5.611	1.00	36.61	A2
ATOM 781 CG1 LEU 104	37.232	70.621	6.381	1.00	39.43	A2
ATOM 782 CG2 LEU 104	37.232	70.621	6.381	1.00	39.43	A2
ATOM 783 C LEU 104	41.904	69.727	6.414	1.00	38.48	A2
ATOM 784 O LEU 104	42.583	69.825	5.398	1.00	28.47	A2
ATOM 785 N ASP 105	42.449	69.949	7.574	1.00	26.79	A2
ATOM 786 C ASP 105	42.449	69.949	7.574	1.00	26.79	A2
ATOM 787 CA ASP 105	43.822	70.307	7.613	1.00	28.67	A2
ATOM 788 CB ASP 105	44.139	70.584	9.038	1.00	36.06	A2
ATOM 789 CD ASP 105	43.822	70.307	7.613	1.00	28.67	A2
ATOM 790 CG1 ASP 105	43.085	72.728	8.339	1.00	35.46	A2
ATOM 791 CG2 ASP 105	43.244	71.816	10.808	1.00	39.10	A2
ATOM 792 C ASP 105	44.301	69.206	7.032	1.00	26.90	A2
ATOM 793 O ASP 105	45.161	69.206	7.032	1.00	26.90	A2
ATOM 794 N THR 106	43.674	67.876	8.019	1.00	0.00	A2
ATOM 795 H THR 106	43.674	67.876	8.019	1.00	0.00	A2
ATOM 796 CA THR 106	45.143	66.770	6.935	1.00	24.81	A2
ATOM 797 CD THR 106	44.301	69.206	7.032	1.00	26.90	A2
ATOM 798 CG1 THR 106	44.680	65.566	8.894	1.00	31.53	A2
ATOM 799 CG2 THR 106	44.069	66.222	9.242	1.00	0.00	A2
ATOM 800 N LEU 107	43.887	66.917	4.946	1.00	24.80	A2
ATOM 801 C LEU 106	45.073	66.412	5.660	1.00	20.90	A2
ATOM 802 O THR 106	46.065	66.412	4.812	1.00	24.68	A2
ATOM 803 N LEU 107	43.684	66.783	5.331	1.00	27.19	A2
ATOM 804 CA LEU 107	42.158	66.913	3.733	1.00	25.45	A2
ATOM 805 CG1 LEU 107	42.395	66.888	1.863	1.00	76.74	A2
ATOM 806 CB LEU 107	40.140	66.925	1.914	1.00	27.62	A2
ATOM 807 CD LEU 107	40.140	66.925	1.914	1.00	27.62	A2
ATOM 808 C LEU 107	44.485	67.848	2.819	1.00	28.01	A2
ATOM 809 O LEU 107	45.161	67.848	2.819	1.00	28.01	A2
ATOM 810 N GLN 108	44.540	69.025	3.373	1.00	18.57	A2
ATOM 811 H GLN 108	44.540	69.025	3.373	1.00	18.57	A2
ATOM 812 CA GLN 108	45.343	70.132	2.795	1.00	28.38	A2

FIGURE 5

ATOM 815 CG	GLN 108	45.318	71.363	3.630	1.00	10.15	A2
ATOM 816 CG	GLN 108	43.711	71.787	3.542	1.00	12.67	A2
ATOM 817 CG	GLN 108	43.006	71.192	4.048	1.00	15.74	A2
ATOM 818 CG	GLN 108	42.295	70.597	4.554	1.00	18.81	A2
ATOM 819 NR2	GLN 108	44.189	74.044	3.213	1.00	31.58	A2
ATOM 820 HE21	GLN 108	44.581	72.701	2.386	1.00	0.00	A2
ATOM 821 C	GLN 108	44.159	69.986	3.471	1.00	0.00	A2
ATOM 822 C	GLN 108	44.159	69.986	3.471	1.00	0.00	A2
ATOM 823 O	GLN 108	47.430	69.955	1.597	1.00	27.57	A2
ATOM 824 N	LEU 109	47.388	69.473	3.833	1.00	25.81	A2
ATOM 825 CA	LEU 109	47.388	69.473	3.833	1.00	25.81	A2
ATOM 826 CB	LEU 109	44.792	69.900	4.915	1.00	27.96	A2
ATOM 827 CG	LEU 109	48.951	68.637	5.513	1.00	29.41	A2
ATOM 828 CD	LEU 109	48.712	69.771	6.570	1.00	31.78	A2
ATOM 829 CE	LEU 109	48.473	69.900	7.628	1.00	34.15	A2
ATOM 830 CD1	LEU 109	49.714	70.889	6.385	1.00	32.19	A2
ATOM 831 C	LEU 109	49.168	67.900	3.186	1.00	26.80	A2
ATOM 832 O	LEU 109	52.214	67.721	2.344	1.00	16.81	A2
ATOM 833 N	LEU 109	48.590	65.664	2.250	1.00	23.32	A2
ATOM 834 H	ASP 110	47.471	66.835	3.600	1.00	0.00	A2
ATOM 835 CA	ASP 110	48.590	65.664	2.250	1.00	23.32	A2
ATOM 836 CB	ASP 110	47.205	64.370	3.954	1.00	31.10	A2
ATOM 837 CG	ASP 110	47.205	64.370	3.954	1.00	31.10	A2
ATOM 838 OD1	ASP 110	47.018	63.093	4.323	1.00	34.98	A2
ATOM 839 OD2	ASP 110	48.951	64.100	4.535	1.00	34.06	A2
ATOM 840 O	ASP 110	48.951	64.100	4.535	1.00	34.06	A2
ATOM 841 O	ASP 110	49.493	65.711	0.165	1.00	20.63	A2
ATOM 842 N	VAL 111	47.627	66.998	0.363	1.00	20.40	A2
ATOM 843 CA	VAL 111	47.627	66.998	0.363	1.00	20.40	A2
ATOM 844 CA	VAL 111	47.731	67.455	1.019	1.00	20.44	A2
ATOM 845 CG	VAL 111	46.531	68.364	-1.376	1.00	23.60	A2
ATOM 846 CD1	VAL 111	46.415	65.946	-1.808	1.00	23.04	A2
ATOM 847 CD2	VAL 111	46.415	65.946	-1.808	1.00	23.04	A2
ATOM 848 C	VAL 111	49.006	68.274	-1.245	1.00	20.82	A2
ATOM 849 O	VAL 111	49.617	68.006	-2.303	1.00	19.22	A2
ATOM 850 N	VAL 111	48.819	69.190	0.492	1.00	20.40	A2
ATOM 851 CA	VAL 111	48.819	69.190	0.492	1.00	20.40	A2
ATOM 852 CA	ALA 112	50.708	69.800	-0.295	1.00	24.16	A2
ATOM 853 CA	ALA 112	50.861	70.561	1.011	1.00	22.69	A2
ATOM 854 CB	ALA 112	51.007	67.417	1.180	1.00	0.00	A2
ATOM 855 O	ALA 112	51.778	69.026	-1.390	1.00	32.53	A2
ATOM 856 N	ASP 113	51.086	67.857	0.343	1.00	30.21	A2
ATOM 857 H	ASP 113	51.507	67.417	1.180	1.00	0.00	A2
ATOM 858 CA	ASP 113	52.706	65.659	0.953	1.00	36.31	A2
ATOM 859 CG	ASP 113	53.170	65.758	2.357	1.00	42.77	A2
ATOM 860 CD	ASP 113	53.700	66.460	3.589	1.00	48.93	A2
ATOM 861 C	ASP 113	54.160	66.460	3.589	1.00	48.93	A2
ATOM 862 O	ASP 113	53.115	66.361	-1.239	1.00	32.82	A2
ATOM 863 N	ASP 113	53.187	66.308	-1.754	1.00	30.75	A2
ATOM 864 O	ASP 113	53.187	66.308	-1.754	1.00	30.75	A2
ATOM 865 O	ASP 113	53.187	66.308	-1.754	1.00	30.75	A2
ATOM 866 H	PIE 114	51.344	66.164	-1.361	1.00	0.00	A2
ATOM 867 CA	PIE 114	51.109	65.128	-3.103	1.00	27.84	A2
ATOM 868 CB	PIE 114	50.708	64.794	-3.216	1.00	21.18	A2
ATOM 869 CD	PIE 114	51.063	63.702	-4.210	1.00	21.04	A2
ATOM 870 CN	PIE 114	51.063	63.702	-4.210	1.00	21.04	A2
ATOM 871 CD1	PIE 114	49.369	63.914	-5.046	1.00	12.47	A2
ATOM 872 CB	PIE 114	51.476	62.514	-6.102	1.00	14.54	A2
ATOM 873 C	PIE 114	50.951	62.514	-6.102	1.00	14.54	A2
ATOM 874 CD	PIE 114	50.951	62.514	-6.102	1.00	14.54	A2
ATOM 875 C	PIE 114	50.951	62.514	-6.102	1.00	14.54	A2
ATOM 876 O	PIE 114	52.453	66.791	-4.190	1.00	27.91	A2
ATOM 877 O	PIE 114	53.072	65.883	-5.158	1.00	30.84	A2
ATOM 878 H	ALA 115	51.446	67.168	-3.117	1.00	0.00	A2
ATOM 879 CA	ALA 115	52.423	68.655	-4.952	1.00	31.29	A2
ATOM 880 CB	ALA 115	53.824	69.939	-4.420	1.00	30.65	A2
ATOM 881 CD	ALA 115	54.531	68.846	-3.813	1.00	27.20	A2
ATOM 882 O	ALA 115	54.539	68.823	-6.004	1.00	30.16	A2
ATOM 883 N	THR 116	54.551	68.846	-3.813	1.00	27.20	A2
ATOM 884 H	THR 116	55.998	68.807	-3.855	1.00	34.91	A2
ATOM 885 CA	THR 116	55.998	68.807	-3.855	1.00	34.91	A2
ATOM 886 CB	THR 116	56.325	68.502	-2.150	1.00	35.78	A2
ATOM 887 CG1	THR 116	55.564	70.018	-1.576	1.00	35.58	A2
ATOM 888 CG2	THR 116	55.564	70.018	-1.576	1.00	35.58	A2
ATOM 889 CD1	THR 116	57.816	69.000	-1.921	1.00	35.58	A2
ATOM 890 C	THR 116	56.714	67.776	-4.304	1.00	37.14	A2
ATOM 891 N	THR 116	56.714	67.776	-4.304	1.00	37.14	A2
ATOM 892 H	THR 116	58.318	66.485	-4.045	1.00	40.05	A2
ATOM 893 H	THR 117	55.615	66.383	-3.369	1.00	0.00	A2
ATOM 894 CA	THR 117	55.615	66.383	-3.369	1.00	0.00	A2
ATOM 895 CB	THR 117	56.149	63.720	-2.820	1.00	41.66	A2
ATOM 896 CG1	THR 117	55.635	64.550	-2.286	1.00	0.00	A2
ATOM 897 CG2	THR 117	55.635	64.550	-2.286	1.00	0.00	A2
ATOM 898 CD1	THR 117	56.887	63.417	-1.334	1.00	41.42	A2
ATOM 899 C	THR 117	56.887	63.417	-1.334	1.00	41.42	A2
ATOM 900 O	THR 117	57.934	63.523	-6.749	1.00	46.79	A2
ATOM 901 N	THR 117	55.983	65.747	-6.741	1.00	45.87	A2
ATOM 902 H	THR 117	55.983	65.747	-6.741	1.00	45.87	A2
ATOM 903 CA	THR 117	55.983	65.747	-6.741	1.00	45.87	A2
ATOM 904 CB	THR 117	55.983	65.747	-6.741	1.00	45.87	A2
ATOM 905 CD	THR 117	55.983	65.747	-6.741	1.00	45.87	A2
ATOM 906 CG1	THR 117	55.983	65.747	-6.741	1.00	45.87	A2
ATOM 907 CG2	THR 117	55.983	65.747	-6.741	1.00	45.87	A2
ATOM 908 C	THR 117	55.983	65.747	-6.741	1.00	45.87	A2
ATOM 909 N	THR 119	56.697	64.081	-4.015	1.00	54.08	A2
ATOM 910 H	THR 119	56.697	64.081	-4.015	1.00	54.08	A2
ATOM 911 H	THR 119	56.697	64.081	-4.015	1.00	54.08	A2
ATOM 912 CA	THR 119	57.934	63.523	-6.749	1.00	46.79	A2
ATOM 913 CB	THR 119	57.934	63.523	-6.749	1.00	46.79	A2
ATOM 914 CG	THR 119	58.051	71.579	-8.196	1.00	62.64	A2
ATOM 915 CD1	THR 119	57.596	72.711	-9.307	1.00	61.78	A2
ATOM 916 CD2	THR 119	58.059	72.953	-9.164	1.00	62.55	A2

FIGURE 5

ATOM 917 C33 TRP 119	56.465	72.114	-10.000	1.00	66.03	A2
ATOM 918 C31 TRP 119	59.322	71.870	-7.863	1.00	64.12	A2
ATOM 919 C32 TRP 119	59.681	72.727	-8.764	1.00	65.00	A2
ATOM 920 C34 TRP 119	58.784	72.814	-10.000	1.00	64.12	A2
ATOM 921 C22 TRP 119	58.726	72.794	-10.174	1.00	62.90	A2
ATOM 922 C23 TRP 119	56.469	72.137	-10.170	1.00	65.18	A2
ATOM 923 C24 TRP 119	56.539	72.887	-11.481	1.00	64.40	A2
ATOM 924 C25 TRP 119	53.539	72.887	-11.481	1.00	64.40	A2
ATOM 925 O TRP 119	53.548	68.788	-3.343	1.00	62.12	A2
ATOM 926 N GIN 120	59.447	64.065	-7.249	1.00	62.91	A2
ATOM 927 C GIN 120	59.447	64.065	-7.249	1.00	62.91	A2
ATOM 928 C GIN 120	60.786	62.504	-7.113	1.00	66.36	A2
ATOM 929 C GIN 120	60.900	66.890	-5.180	1.00	66.36	A2
ATOM 930 CG GIN 120	60.627	67.678	-4.582	1.00	67.18	A2
ATOM 931 CG GIN 120	60.627	67.678	-4.582	1.00	67.18	A2
ATOM 932 CG GIN 120	60.627	67.678	-4.582	1.00	67.18	A2
ATOM 933 NE2 GIN 120	60.308	65.634	-3.129	1.00	69.31	A2
ATOM 934 NE1 GIN 120	61.221	67.465	-2.129	1.00	69.31	A2
ATOM 935 C GIN 120	61.169	66.509	-2.122	1.00	66.32	A2
ATOM 936 C GIN 120	61.169	66.509	-2.122	1.00	66.32	A2
ATOM 937 O GIN 120	62.226	66.421	-4.662	1.00	66.30	A2
ATOM 938 C GIN 120	62.226	66.421	-4.662	1.00	66.30	A2
ATOM 939 N GIN 121	59.291	63.971	-10.070	1.00	67.96	A2
ATOM 940 C GIN 121	60.480	64.878	-9.812	1.00	68.86	A2
ATOM 941 C GIN 121	60.480	64.878	-9.812	1.00	68.86	A2
ATOM 942 C GIN 121	60.480	64.878	-9.812	1.00	68.86	A2
ATOM 943 C GIN 121	60.940	62.226	-10.851	1.00	71.37	A2
ATOM 944 OE1 GIN 121	61.212	61.706	-9.777	1.00	71.70	A2
ATOM 945 OE2 GIN 121	61.212	62.729	-11.786	1.00	71.70	A2
ATOM 946 HIE2 GIN 121	61.212	62.729	-11.786	1.00	71.70	A2
ATOM 947 HIE2 GIN 121	61.236	61.959	-11.541	1.00	0.00	A2
ATOM 948 C GIN 121	60.750	63.743	-11.045	1.00	70.48	A2
ATOM 949 C GIN 121	60.750	63.743	-11.045	1.00	70.48	A2
ATOM 950 N MET 122	60.019	66.846	-11.236	1.00	71.67	A2
ATOM 951 N MET 122	59.351	67.087	-10.555	1.00	0.00	A2
ATOM 952 CA MET 122	60.190	67.688	-12.412	1.00	72.62	A2
ATOM 953 CA MET 122	60.190	67.688	-12.412	1.00	72.62	A2
ATOM 954 CG MET 122	57.880	64.343	-13.083	1.00	73.64	A2
ATOM 955 SD MET 122	56.669	66.662	-13.395	1.00	75.44	A2
ATOM 956 SD MET 122	56.669	66.662	-13.395	1.00	75.44	A2
ATOM 957 C MET 122	61.566	68.281	-12.411	1.00	73.72	A2
ATOM 958 O MET 122	62.240	68.281	-12.441	1.00	73.63	A2
ATOM 959 N GIN 123	61.591	68.697	-11.223	1.00	74.74	A2
ATOM 960 C GIN 123	62.841	71.529	-4.122	1.00	13.02	A2
ATOM 961 CA GIN 123	63.305	69.262	-11.018	1.00	75.95	A2
ATOM 962 CG GIN 123	63.444	69.665	-9.597	1.00	75.72	A2
ATOM 963 CG GIN 123	62.841	71.529	-4.122	1.00	13.02	A2
ATOM 964 OE2 GIN 123	62.741	72.763	-8.057	1.00	84.45	A2
ATOM 965 OE1 GIN 123	62.544	70.789	-7.133	1.00	84.45	A2
ATOM 966 C GIN 123	64.381	68.280	-11.386	1.00	71.17	A2
ATOM 967 C GIN 123	64.381	68.280	-11.386	1.00	71.17	A2
ATOM 968 O GIN 123	64.381	68.280	-11.386	1.00	71.17	A2
ATOM 969 N GIN 123	64.381	68.280	-11.386	1.00	71.17	A2
ATOM 970 N GIN 124	64.381	68.280	-11.386	1.00	71.17	A2
ATOM 971 CG GIN 124	64.381	68.280	-11.386	1.00	71.17	A2
ATOM 972 CG GIN 124	64.381	68.280	-11.386	1.00	71.17	A2
ATOM 973 CG GIN 124	64.381	68.280	-11.386	1.00	71.17	A2
ATOM 974 CG GIN 124	64.381	68.280	-11.386	1.00	71.17	A2
ATOM 975 CG GIN 124	64.381	68.280	-11.386	1.00	71.17	A2
ATOM 976 CG GIN 124	64.381	68.280	-11.386	1.00	71.17	A2
ATOM 977 C GIN 124	64.381	68.280	-11.386	1.00	71.17	A2
ATOM 978 O GIN 124	64.381	68.280	-11.386	1.00	71.17	A2
ATOM 979 C GIN 125	64.381	68.280	-11.386	1.00	71.17	A2
ATOM 980 N LBU 125	64.381	68.280	-11.386	1.00	71.17	A2
ATOM 981 CA LBU 125	64.381	68.280	-11.386	1.00	71.17	A2
ATOM 982 CG LBU 125	64.381	68.280	-11.386	1.00	71.17	A2
ATOM 983 CG LBU 125	64.381	68.280	-11.386	1.00	71.17	A2
ATOM 984 CD LBU 125	64.381	68.280	-11.386	1.00	71.17	A2
ATOM 985 CD LBU 125	64.381	68.280	-11.386	1.00	71.17	A2
ATOM 986 N LBU 126	64.381	68.280	-11.386	1.00	71.17	A2
ATOM 987 O LBU 126	64.381	68.280	-11.386	1.00	71.17	A2
ATOM 988 N GIN 126	64.381	68.280	-11.386	1.00	71.17	A2
ATOM 989 CG GIN 126	64.381	68.280	-11.386	1.00	71.17	A2
ATOM 990 CG GIN 126	64.381	68.280	-11.386	1.00	71.17	A2
ATOM 991 C GIN 126	64.381	68.280	-11.386	1.00	71.17	A2
ATOM 992 O GIN 126	64.381	68.280	-11.386	1.00	71.17	A2
ATOM 993 C GIN 126	64.381	68.280	-11.386	1.00	71.17	A2
ATOM 994 N MET 127	64.381	68.280	-11.386	1.00	71.17	A2
ATOM 995 CA MET 127	64.381	68.280	-11.386	1.00	71.17	A2
ATOM 996 CG MET 127	64.381	68.280	-11.386	1.00	71.17	A2
ATOM 997 CG MET 127	64.381	68.280	-11.386	1.00	71.17	A2
ATOM 998 SD MET 127	64.381	68.280	-11.386	1.00	71.17	A2
ATOM 999 CE MET 127	64.381	68.280	-11.386	1.00	71.17	A2
ATOM 1000 CE MET 127	64.381	68.280	-11.386	1.00	71.17	A2
ATOM 1001 OT1 MET 127	64.381	68.280	-11.386	1.00	71.17	A2
ATOM 1002 OT2 MET 127	64.381	68.280	-11.386	1.00	71.17	A2
ATOM 1003 CE MET 128	64.381	68.280	-11.386	1.00	71.17	A2
ATOM 1004 CE MET 128	64.381	68.280	-11.386	1.00	71.17	A2
ATOM 1005 SD MET 128	64.381	68.280	-11.386	1.00	71.17	A2
ATOM 1006 CE MET 128	64.381	68.280	-11.386	1.00	71.17	A2
ATOM 1007 CE MET 128	64.381	68.280	-11.386	1.00	71.17	A2
ATOM 1008 O MET 128	64.381	68.280	-11.386	1.00	71.17	A2
ATOM 1009 HT1 MET 128	64.381	68.280	-11.386	1.00	71.17	A2
ATOM 1010 HT2 MET 128	64.381	68.280	-11.386	1.00	71.17	A2
ATOM 1011 HT3 MET 128	64.381	68.280	-11.386	1.00	71.17	A2
ATOM 1012 HT3 MET 128	64.381	68.280	-11.386	1.00	71.17	A2
ATOM 1013 CA MET 128	64.381	68.280	-11.386	1.00	71.17	A2
ATOM 1014 CA MET 128	64.381	68.280	-11.386	1.00	71.17	A2
ATOM 1015 CD PRO 129	64.381	68.280	-11.386	1.00	71.17	A2
ATOM 1016 CA PRO 129	64.381	68.280	-11.386	1.00	71.17	A2
ATOM 1017 C PRO 129	64.381	68.280	-11.386	1.00	71.17	A2
ATOM 1018 CG PRO 129	64.381	68.280	-11.386	1.00	71.17	A2

FIGURE 5

ATOM 1019 C	PRO	139	34.588	80.873	-3.664	1.00	512.4	A3
ATOM 1020 C	PHO	139	35.507	80.623	-2.882	1.00	511.89	A3
ATOM 1021 N	ALA	140	33.499	81.547	-3.742	1.00	40.86	A3
ATOM 1022 CA	ALA	140	33.234	81.926	-3.994	1.00	49.19	A3
ATOM 1023 CA	ALA	140	33.234	81.926	-3.994	1.00	49.19	A3
ATOM 1024 CB	ALA	140	32.966	83.413	-1.895	1.00	67.94	A3
ATOM 1025 C	ALA	140	32.978	81.135	-1.590	1.00	49.25	A3
ATOM 1026 CA	ALA	140	32.978	81.135	-1.590	1.00	49.25	A3
ATOM 1027 N	PHE	141	32.793	80.441	-0.506	1.00	41.48	A3
ATOM 1028 H	PHE	141	33.190	80.550	-0.122	1.00	0.00	A3
ATOM 1029 CA	PHE	141	32.752	82.027	-0.710	1.00	40.66	A3
ATOM 1030 CB	PHE	141	32.752	82.027	-0.710	1.00	40.66	A3
ATOM 1031 CG	PHE	141	32.684	77.404	-0.149	1.00	33.35	A3
ATOM 1032 CD	PHE	141	31.800	76.591	-1.006	1.00	34.49	A3
ATOM 1033 CE	PHE	141	31.800	76.591	-1.006	1.00	34.49	A3
ATOM 1034 CB	PHE	141	32.752	75.895	-2.133	1.00	14.44	A3
ATOM 1035 CE2	PHE	141	34.358	76.807	-0.956	1.00	36.69	A3
ATOM 1036 C2	PHE	141	33.449	76.001	-2.614	1.00	37.29	A3
ATOM 1037 N	ALA	142	33.449	76.001	-2.614	1.00	37.29	A3
ATOM 1038 N	ALA	142	33.449	76.001	-2.614	1.00	37.29	A3
ATOM 1039 N	ALA	142	30.867	81.452	0.843	1.00	47.38	A3
ATOM 1040 H	ALA	142	29.624	81.795	-0.010	1.00	0.00	A3
ATOM 1041 CA	ALA	142	28.703	82.546	0.879	1.00	45.04	A3
ATOM 1042 CB	ALA	142	28.703	82.546	0.879	1.00	45.04	A3
ATOM 1043 C	ALA	142	28.703	82.546	0.879	1.00	45.04	A3
ATOM 1044 N	SER	143	28.703	82.546	0.879	1.00	45.04	A3
ATOM 1045 N	SER	143	28.703	82.546	0.879	1.00	45.04	A3
ATOM 1046 H	SER	143	28.703	82.546	0.879	1.00	45.04	A3
ATOM 1047 CA	SER	143	27.337	80.392	3.897	1.00	41.94	A3
ATOM 1048 CB	SER	143	27.337	80.392	3.897	1.00	41.94	A3
ATOM 1049 CG	SER	143	27.337	80.392	3.897	1.00	41.94	A3
ATOM 1050 CG	SER	143	27.337	80.392	3.897	1.00	41.94	A3
ATOM 1051 C	SER	143	27.337	80.392	3.897	1.00	41.94	A3
ATOM 1052 N	ALA	144	27.337	80.392	3.897	1.00	41.94	A3
ATOM 1053 N	ALA	144	27.337	80.392	3.897	1.00	41.94	A3
ATOM 1054 H	ALA	144	26.449	75.312	5.960	1.00	0.00	A3
ATOM 1055 CA	ALA	144	26.449	75.312	5.960	1.00	0.00	A3
ATOM 1056 CB	ALA	144	26.449	75.312	5.960	1.00	0.00	A3
ATOM 1057 C	ALA	144	26.964	76.407	5.677	1.00	41.58	A3
ATOM 1058 O	ALA	144	27.706	75.444	-3.444	1.00	41.07	A3
ATOM 1059 H	ALA	144	25.149	77.203	5.110	1.00	0.00	A3
ATOM 1060 H	PHE	145	25.149	77.203	5.110	1.00	0.00	A3
ATOM 1061 CA	PHE	145	25.307	75.234	4.312	1.00	39.31	A3
ATOM 1062 CB	PHE	145	25.307	75.234	4.312	1.00	39.31	A3
ATOM 1063 CG	PHE	145	23.477	74.452	2.641	1.00	11.91	A3
ATOM 1064 CD	PHE	145	23.477	74.452	2.641	1.00	11.91	A3
ATOM 1065 CD2	PHE	145	23.013	73.183	2.916	1.00	75.40	A3
ATOM 1066 CE	PHE	145	22.661	72.189	1.858	1.00	28.80	A3
ATOM 1067 CE1	PHE	145	22.661	72.189	1.858	1.00	28.80	A3
ATOM 1068 C2	PHE	145	22.764	72.071	0.549	1.00	36.58	A3
ATOM 1069 C	PHE	145	22.764	72.071	0.549	1.00	36.58	A3
ATOM 1070 C	PHE	145	22.764	72.071	0.549	1.00	36.58	A3
ATOM 1071 O	PHE	145	26.556	73.918	2.107	1.00	10.55	A3
ATOM 1072 N	GIN	146	26.475	76.121	2.415	1.00	10.55	A3
ATOM 1073 CA	GIN	146	26.475	76.121	2.415	1.00	10.55	A3
ATOM 1074 CB	GIN	146	26.475	76.121	2.415	1.00	10.55	A3
ATOM 1075 CG	GIN	146	26.475	76.121	2.415	1.00	10.55	A3
ATOM 1076 CD	GIN	146	26.475	76.121	2.415	1.00	10.55	A3
ATOM 1077 CE	GIN	146	26.475	76.121	2.415	1.00	10.55	A3
ATOM 1078 NE2	GIN	146	26.475	76.121	2.415	1.00	10.55	A3
ATOM 1079 NE21	GIN	146	26.475	76.121	2.415	1.00	10.55	A3
ATOM 1080 NE22	GIN	146	26.475	76.121	2.415	1.00	10.55	A3
ATOM 1081 N	ARG	147	26.475	76.121	2.415	1.00	10.55	A3
ATOM 1082 O	GIN	146	26.475	76.121	2.415	1.00	10.55	A3
ATOM 1083 N	ARG	147	26.475	76.121	2.415	1.00	10.55	A3
ATOM 1084 H	ARG	147	26.475	76.121	2.415	1.00	10.55	A3
ATOM 1085 CB	ARG	147	26.475	76.121	2.415	1.00	10.55	A3
ATOM 1086 CG	ARG	147	26.475	76.121	2.415	1.00	10.55	A3
ATOM 1087 CG	ARG	147	26.475	76.121	2.415	1.00	10.55	A3
ATOM 1088 CE	ARG	147	26.475	76.121	2.415	1.00	10.55	A3
ATOM 1089 NE	ARG	147	26.475	76.121	2.415	1.00	10.55	A3
ATOM 1090 HE	ARG	147	26.475	76.121	2.415	1.00	10.55	A3
ATOM 1091 CE	ARG	147	26.475	76.121	2.415	1.00	10.55	A3
ATOM 1092 N	ARG	147	26.475	76.121	2.415	1.00	10.55	A3
ATOM 1093 H111	ARG	147	26.475	76.121	2.415	1.00	10.55	A3
ATOM 1094 H112	ARG	147	26.475	76.121	2.415	1.00	10.55	A3
ATOM 1095 H113	ARG	147	26.475	76.121	2.415	1.00	10.55	A3
ATOM 1096 H114	ARG	147	26.475	76.121	2.415	1.00	10.55	A3
ATOM 1097 H115	ARG	147	26.475	76.121	2.415	1.00	10.55	A3
ATOM 1098 C	ARG	147	26.475	76.121	2.415	1.00	10.55	A3
ATOM 1099 N	ALA	148	26.475	76.121	2.415	1.00	10.55	A3
ATOM 1100 N	ALA	148	26.475	76.121	2.415	1.00	10.55	A3
ATOM 1101 H	ALA	148	26.475	76.121	2.415	1.00	10.55	A3
ATOM 1102 CA	ALA	148	26.475	76.121	2.415	1.00	10.55	A3
ATOM 1103 CB	ALA	148	26.475	76.121	2.415	1.00	10.55	A3
ATOM 1104 C	ALA	148	26.475	76.121	2.415	1.00	10.55	A3
ATOM 1105 O	ALA	148	26.475	76.121	2.415	1.00	10.55	A3
ATOM 1106 N	ALA	149	26.475	76.121	2.415	1.00	10.55	A3
ATOM 1107 H	ALA	149	26.475	76.121	2.415	1.00	10.55	A3
ATOM 1108 CA	ALA	149	26.475	76.121	2.415	1.00	10.55	A3
ATOM 1109 CB	ALA	149	26.475	76.121	2.415	1.00	10.55	A3
ATOM 1110 C	ALA	149	26.475	76.121	2.415	1.00	10.55	A3
ATOM 1111 O	ALA	149	26.475	76.121	2.415	1.00	10.55	A3
ATOM 1112 N	GLY	150	26.475	76.121	2.415	1.00	10.55	A3
ATOM 1113 CA	GLY	150	26.475	76.121	2.415	1.00	10.55	A3
ATOM 1114 CB	GLY	150	26.475	76.121	2.415	1.00	10.55	A3
ATOM 1115 C	GLY	150	26.475	76.121	2.415	1.00	10.55	A3
ATOM 1116 O	GLY	150	26.475	76.121	2.415	1.00	10.55	A3
ATOM 1117 N	GLY	151	26.475	76.121	2.415	1.00	10.55	A3
ATOM 1118 H	GLY	151	26.475	76.121	2.415	1.00	10.55	A3
ATOM 1119 CA	GLY	151	26.475	76.121	2.415	1.00	10.55	A3
ATOM 1120 C	GLY	151	26.475	76.121	2.415	1.00	10.55	A3

FIGURE 5

ATOM 1121 O GLY 151	33.664	68.501	-0.349	1.00	35.66	A3
ATOM 1122 N VAL 152	31.486	64.418	0.451	1.00	31.87	A3
ATOM 1123 CA VAL 152	30.919	67.240	0.000	1.00	31.00	A3
ATOM 1124 CB VAL 152	30.919	67.240	0.000	1.00	31.00	A3
ATOM 1125 CG VAL 152	29.419	67.145	-0.125	1.00	27.63	A3
ATOM 1126 CD VAL 152	28.883	66.035	-0.976	1.00	27.37	A3
ATOM 1127 CE VAL 152	28.883	66.035	-0.976	1.00	27.37	A3
ATOM 1128 O VAL 151	31.805	66.236	-1.719	1.00	44.74	A3
ATOM 1129 C VAL 152	31.805	66.236	-1.719	1.00	31.75	A3
ATOM 1130 N LEU 153	31.236	64.451	-2.361	1.00	29.26	A3
ATOM 1131 CA LEU 153	31.559	64.607	-1.760	1.00	29.27	A3
ATOM 1132 CB LEU 153	31.559	64.607	-1.760	1.00	29.27	A3
ATOM 1133 CD LEU 153	30.881	69.858	-4.160	1.00	28.22	A3
ATOM 1134 CE LEU 153	30.881	69.858	-4.160	1.00	28.22	A3
ATOM 1135 CG LEU 153	29.941	71.365	-5.996	1.00	14.46	A3
ATOM 1136 CD LEU 153	29.941	71.365	-5.996	1.00	14.46	A3
ATOM 1137 C LEU 153	32.032	64.421	-5.111	1.00	26.08	A3
ATOM 1138 N VAL 154	31.419	64.187	-5.212	1.00	26.78	A3
ATOM 1139 CA VAL 154	31.389	69.557	-2.416	1.00	0.00	A3
ATOM 1140 CB VAL 154	31.389	69.557	-2.416	1.00	0.00	A3
ATOM 1141 CD VAL 154	35.330	69.239	-3.611	1.00	26.23	A3
ATOM 1142 CE VAL 154	35.330	69.239	-3.611	1.00	26.23	A3
ATOM 1143 CG VAL 154	35.330	69.239	-3.611	1.00	26.23	A3
ATOM 1144 CD VAL 154	35.330	69.239	-3.611	1.00	26.23	A3
ATOM 1145 CE VAL 154	35.330	69.239	-3.611	1.00	26.23	A3
ATOM 1146 CG VAL 154	35.330	69.239	-3.611	1.00	26.23	A3
ATOM 1147 N ALA 155	35.933	67.450	-3.375	1.00	26.80	A3
ATOM 1148 CA ALA 155	35.685	67.451	-2.199	1.00	24.76	A3
ATOM 1149 CB ALA 155	35.685	67.451	-2.199	1.00	24.76	A3
ATOM 1150 CD ALA 155	35.095	65.940	-0.782	1.00	25.21	A3
ATOM 1151 CE ALA 155	35.095	65.940	-0.782	1.00	25.21	A3
ATOM 1152 O ALA 155	35.708	64.946	-2.841	1.00	26.94	A3
ATOM 1153 CA SER 156	36.594	64.888	-3.398	1.00	26.76	A3
ATOM 1154 CB SER 156	36.594	64.888	-3.398	1.00	26.76	A3
ATOM 1155 CG SER 156	31.790	65.577	-2.466	1.00	0.00	A3
ATOM 1156 CD SER 156	31.790	65.577	-2.466	1.00	0.00	A3
ATOM 1157 CE SER 156	34.034	64.105	-4.354	1.00	31.17	A3
ATOM 1158 CG SER 156	34.034	64.105	-4.354	1.00	31.17	A3
ATOM 1159 CD SER 156	31.170	63.115	-5.851	1.00	0.00	A3
ATOM 1160 CE SER 156	31.170	63.115	-5.851	1.00	0.00	A3
ATOM 1161 N HIS 157	34.445	64.338	-5.532	1.00	33.46	A3
ATOM 1162 CA HIS 157	34.771	66.349	-5.605	1.00	0.00	A3
ATOM 1163 CB HIS 157	34.771	66.349	-5.605	1.00	0.00	A3
ATOM 1164 CD HIS 157	35.821	65.773	-7.383	1.00	31.19	A3
ATOM 1165 CE HIS 157	35.821	65.773	-7.383	1.00	31.19	A3
ATOM 1166 CG HIS 157	34.269	67.449	-4.866	1.00	31.11	A3
ATOM 1167 CD HIS 157	34.269	67.449	-4.866	1.00	31.11	A3
ATOM 1168 CE HIS 157	34.137	67.394	-9.918	1.00	30.78	A3
ATOM 1169 CD HIS 157	34.137	67.394	-9.918	1.00	30.78	A3
ATOM 1170 CE HIS 157	32.993	67.232	-8.873	1.00	32.01	A3
ATOM 1171 CD HIS 157	32.993	67.232	-8.873	1.00	32.01	A3
ATOM 1172 CE HIS 157	31.327	67.281	-10.879	1.00	0.00	A3
ATOM 1173 O HIS 157	31.327	67.281	-10.879	1.00	0.00	A3
ATOM 1174 N LEU 158	37.401	65.969	-6.071	1.00	29.24	A3
ATOM 1175 CA LEU 158	37.401	65.969	-6.071	1.00	29.24	A3
ATOM 1176 CB LEU 158	37.401	65.969	-6.071	1.00	29.24	A3
ATOM 1177 CD LEU 158	37.401	65.969	-6.071	1.00	29.24	A3
ATOM 1178 CE LEU 158	37.401	65.969	-6.071	1.00	29.24	A3
ATOM 1179 CG LEU 158	37.401	65.969	-6.071	1.00	29.24	A3
ATOM 1180 CD LEU 158	37.401	65.969	-6.071	1.00	29.24	A3
ATOM 1181 C LEU 158	37.401	65.969	-6.071	1.00	29.24	A3
ATOM 1182 O LEU 158	37.401	65.969	-6.071	1.00	29.24	A3
ATOM 1183 N LEU 158	37.401	65.969	-6.071	1.00	29.24	A3
ATOM 1184 CA LEU 158	37.401	65.969	-6.071	1.00	29.24	A3
ATOM 1185 CB LEU 158	37.401	65.969	-6.071	1.00	29.24	A3
ATOM 1186 CD LEU 158	37.401	65.969	-6.071	1.00	29.24	A3
ATOM 1187 CE LEU 158	37.401	65.969	-6.071	1.00	29.24	A3
ATOM 1188 CG LEU 158	37.401	65.969	-6.071	1.00	29.24	A3
ATOM 1189 CD LEU 158	37.401	65.969	-6.071	1.00	29.24	A3
ATOM 1190 CE LEU 158	37.401	65.969	-6.071	1.00	29.24	A3
ATOM 1191 CG LEU 158	37.401	65.969	-6.071	1.00	29.24	A3
ATOM 1192 CD LEU 158	37.401	65.969	-6.071	1.00	29.24	A3
ATOM 1193 C LEU 158	37.401	65.969	-6.071	1.00	29.24	A3
ATOM 1194 N SER 160	37.401	65.969	-6.071	1.00	29.24	A3
ATOM 1195 CA SER 160	37.401	65.969	-6.071	1.00	29.24	A3
ATOM 1196 CB SER 160	37.401	65.969	-6.071	1.00	29.24	A3
ATOM 1197 CD SER 160	37.401	65.969	-6.071	1.00	29.24	A3
ATOM 1198 CE SER 160	37.401	65.969	-6.071	1.00	29.24	A3
ATOM 1199 CG SER 160	37.401	65.969	-6.071	1.00	29.24	A3
ATOM 1200 CD SER 160	37.401	65.969	-6.071	1.00	29.24	A3
ATOM 1201 C SER 160	37.401	65.969	-6.071	1.00	29.24	A3
ATOM 1202 N PHE 161	39.303	63.796	-8.864	1.00	33.82	A3
ATOM 1203 CA PHE 161	39.303	63.796	-8.864	1.00	33.82	A3
ATOM 1204 CB PHE 161	39.303	63.796	-8.864	1.00	33.82	A3
ATOM 1205 CD PHE 161	39.303	63.796	-8.864	1.00	33.82	A3
ATOM 1206 CE PHE 161	39.303	63.796	-8.864	1.00	33.82	A3
ATOM 1207 CG PHE 161	39.303	63.796	-8.864	1.00	33.82	A3
ATOM 1208 CD PHE 161	39.303	63.796	-8.864	1.00	33.82	A3
ATOM 1209 CE PHE 161	39.303	63.796	-8.864	1.00	33.82	A3
ATOM 1210 CG PHE 161	39.303	63.796	-8.864	1.00	33.82	A3
ATOM 1211 CD PHE 161	39.303	63.796	-8.864	1.00	33.82	A3
ATOM 1212 CE PHE 161	39.303	63.796	-8.864	1.00	33.82	A3
ATOM 1213 C PHE 161	39.303	63.796	-8.864	1.00	33.82	A3
ATOM 1214 O PHE 161	39.303	63.796	-8.864	1.00	33.82	A3
ATOM 1215 N LEU 162	42.786	62.578	-10.845	1.00	31.77	A3
ATOM 1216 CA LEU 162	42.786	62.578	-10.845	1.00	31.77	A3
ATOM 1217 CB LEU 162	42.786	62.578	-10.845	1.00	31.77	A3
ATOM 1218 CD LEU 162	42.786	62.578	-10.845	1.00	31.77	A3
ATOM 1219 CE LEU 162	42.786	62.578	-10.845	1.00	31.77	A3
ATOM 1220 CG LEU 162	42.786	62.578	-10.845	1.00	31.77	A3
ATOM 1221 CD LEU 162	42.786	62.578	-10.845	1.00	31.77	A3
ATOM 1222 C LEU 162	42.786	62.578	-10.845	1.00	31.77	A3

FIGURE 5

ATOM 1223 O LBU 163	46.087	59.654	-9.070	1.00	16.51	A3
ATOM 1224 N GLU 163	41.072	60.002	-8.816	1.00	0.00	A1
ATOM 1225 N GLU 163	41.975	58.327	-9.771	1.00	-0.47	A3
ATOM 1226 CA GLU 163	40.784	56.275	-10.055	1.00	-0.48	A3
ATOM 1227 CG GLU 163	40.784	56.275	-10.055	1.00	-0.48	A3
ATOM 1228 CG GLU 163	41.291	55.889	-8.126	1.00	5.97	A3
ATOM 1229 CD GLU 163	40.897	54.721	-8.092	1.00	6.01	A3
ATOM 1230 OE GLU 163	40.897	54.721	-8.092	1.00	6.01	A3
ATOM 1231 O LBU 163	42.386	58.420	-11.143	1.00	-0.17	A3
ATOM 1232 C GLU 163	43.456	57.633	-11.486	1.00	-0.17	A3
ATOM 1233 O GLU 163	41.257	59.636	-11.930	1.00	-0.28	A3
ATOM 1234 N VAL 164	41.911	59.609	-13.187	1.00	-0.52	A3
ATOM 1235 CA VAL 164	41.207	60.711	-13.940	1.00	-0.52	A3
ATOM 1236 CG VAL 164	41.207	60.711	-13.940	1.00	-0.52	A3
ATOM 1237 CD VAL 164	41.207	60.711	-13.940	1.00	-0.52	A3
ATOM 1238 CE VAL 164	41.207	60.711	-13.940	1.00	-0.52	A3
ATOM 1239 CG VAL 164	41.207	60.711	-13.940	1.00	-0.52	A3
ATOM 1240 C VAL 164	44.386	59.933	-12.991	1.00	-0.61	A3
ATOM 1241 O VAL 164	45.193	59.473	-13.794	1.00	-0.59	A3
ATOM 1244 CA SER 165	46.325	60.845	-11.895	1.00	5.44	A3
ATOM 1245 CG SER 165	46.325	60.845	-11.895	1.00	5.44	A3
ATOM 1246 CD SER 165	46.047	60.984	-9.361	1.00	0.00	A3
ATOM 1247 CG SER 165	45.997	60.984	-9.361	1.00	0.00	A3
ATOM 1248 C SER 165	46.958	58.502	-11.610	1.00	5.15	A3
ATOM 1249 N THR 166	46.319	58.645	-10.900	1.00	5.57	A3
ATOM 1250 N THR 166	45.374	58.948	-10.549	1.00	0.00	A3
ATOM 1251 C THR 166	45.541	57.773	-10.625	1.00	6.41	A3
ATOM 1252 CG THR 166	45.541	57.773	-10.625	1.00	6.41	A3
ATOM 1253 CD THR 166	45.501	55.138	-9.682	1.00	69.00	A3
ATOM 1254 CG THR 166	44.389	54.501	-10.185	1.00	71.64	A3
ATOM 1255 CD THR 166	44.389	54.501	-10.185	1.00	71.64	A3
ATOM 1256 CE THR 166	46.594	54.009	-9.257	1.00	71.27	A3
ATOM 1257 CD THR 166	46.594	54.009	-9.257	1.00	71.27	A3
ATOM 1258 CE THR 166	45.463	51.417	-8.882	1.00	75.71	A3
ATOM 1259 CD THR 166	45.463	51.417	-8.882	1.00	75.71	A3
ATOM 1260 BH THR 166	46.712	56.567	-11.987	1.00	62.34	A3
ATOM 1262 C THR 166	46.712	56.567	-11.987	1.00	62.34	A3
ATOM 1263 N THR 166	45.913	55.982	-14.519	1.00	61.47	A3
ATOM 1264 N ALA 167	45.913	55.982	-14.519	1.00	61.47	A3
ATOM 1265 N ALA 167	44.893	57.089	-12.678	1.00	0.00	A3
ATOM 1266 C ALA 167	45.913	55.982	-14.519	1.00	61.47	A3
ATOM 1267 N ALA 167	45.913	55.982	-14.519	1.00	61.47	A3
ATOM 1268 C ALA 167	46.982	56.694	-15.020	1.00	62.19	A3
ATOM 1269 O ALA 167	47.719	56.000	-15.734	1.00	62.63	A3
ATOM 1270 N VAL 168	46.736	58.570	-14.100	1.00	8.00	A3
ATOM 1271 C VAL 168	46.736	58.570	-14.100	1.00	8.00	A3
ATOM 1272 N VAL 168	46.736	58.570	-14.100	1.00	8.00	A3
ATOM 1273 C VAL 168	48.061	60.121	-16.131	1.00	66.30	A3
ATOM 1274 CG VAL 168	46.487	60.431	-16.706	1.00	66.78	A1
ATOM 1275 CG VAL 168	46.487	60.431	-16.706	1.00	66.78	A1
ATOM 1276 N LBU 169	46.979	58.339	-15.400	1.00	66.45	A1
ATOM 1277 O VAL 169	50.453	58.241	-14.177	1.00	66.84	A1
ATOM 1278 N LBU 169	49.823	58.339	-14.177	1.00	66.84	A1
ATOM 1279 CG LBU 169	49.102	58.404	-13.536	1.00	0.00	A1
ATOM 1280 CD LBU 169	51.249	58.328	-12.188	1.00	71.51	A1
ATOM 1281 CE LBU 169	51.249	58.328	-12.188	1.00	71.51	A1
ATOM 1282 CG LBU 169	51.137	59.732	-11.813	1.00	76.68	A1
ATOM 1283 CD LBU 169	51.137	59.732	-11.813	1.00	76.68	A1
ATOM 1284 CE LBU 169	51.237	59.826	-10.798	1.00	60.09	A1
ATOM 1285 C LBU 169	51.333	56.414	-13.978	1.00	71.61	A1
ATOM 1286 Q LBU 169	51.408	56.013	-14.429	1.00	74.55	A1
ATOM 1287 O LBU 169	51.408	56.013	-14.429	1.00	74.55	A1
ATOM 1288 Q LBU 169	49.408	55.923	-13.179	1.00	75.45	A1
ATOM 1289 CA ARG 170	50.364	54.179	-14.199	1.00	78.17	A3
ATOM 1290 CG ARG 170	48.944	53.642	-14.004	1.00	78.45	A3
ATOM 1291 CD ARG 170	48.944	53.642	-14.004	1.00	78.45	A3
ATOM 1292 CE ARG 170	48.944	53.642	-14.004	1.00	78.45	A3
ATOM 1293 NE ARG 170	48.123	51.120	-12.970	1.00	76.15	A3
ATOM 1294 CG ARG 170	48.123	51.120	-12.970	1.00	76.15	A3
ATOM 1295 CD ARG 170	48.123	51.120	-12.970	1.00	76.15	A3
ATOM 1296 NH ARG 170	48.758	50.547	-11.974	1.00	0.00	A3
ATOM 1297 NH ARG 170	48.758	50.547	-11.974	1.00	0.00	A3
ATOM 1298 NH ARG 170	50.441	50.030	-12.294	1.00	0.00	A3
ATOM 1299 NH ARG 170	50.441	50.030	-12.294	1.00	0.00	A3
ATOM 1299 NH ARG 170	48.147	50.492	-10.806	1.00	72.02	A3
ATOM 1300 NH ARG 170	48.147	50.492	-10.806	1.00	72.02	A3
ATOM 1301 C ARG 170	51.914	53.470	-15.908	1.00	81.07	A3
ATOM 1302 C ARG 170	50.810	54.072	-15.643	1.00	80.00	A3
ATOM 1303 O ARG 170	51.914	53.470	-15.908	1.00	81.07	A3
ATOM 1304 N HIS 171	40.433	55.663	-16.411	1.00	81.18	A1
ATOM 1305 N HIS 171	40.433	55.663	-16.411	1.00	81.18	A1
ATOM 1306 CA HIS 171	50.663	54.597	-17.970	1.00	84.03	A3
ATOM 1307 CG HIS 171	48.590	55.054	-18.903	1.00	86.82	A3
ATOM 1308 CD HIS 171	48.590	55.054	-18.903	1.00	86.82	A3
ATOM 1309 CE HIS 171	47.467	53.765	-18.272	1.00	91.73	A3
ATOM 1310 NH HIS 171	48.308	53.301	-20.248	1.00	92.74	A3
ATOM 1311 NH HIS 171	48.308	53.301	-20.248	1.00	92.74	A3
ATOM 1312 CE HIS 171	48.887	53.387	-21.044	1.00	0.00	A3
ATOM 1313 NE HIS 171	46.711	52.892	-18.899	1.00	92.59	A3
ATOM 1314 BE HIS 171	45.884	53.531	-18.518	1.00	0.00	A3
ATOM 1316 O HIS 171	51.440	55.357	-19.144	1.00	85.47	A3
ATOM 1317 N LBU 172	52.359	56.480	-17.321	1.00	86.13	A3
ATOM 1318 N LBU 172	52.359	56.480	-17.321	1.00	86.13	A3
ATOM 1319 CA LBU 172	53.506	54.371	-16.403	1.00	0.00	A3
ATOM 1320 CG LBU 172	53.506	54.371	-16.403	1.00	0.00	A3
ATOM 1321 CD LBU 172	54.021	59.658	-17.203	1.00	87.48	A1
ATOM 1322 CE LBU 172	54.021	59.658	-17.203	1.00	87.48	A1
ATOM 1323 CD LBU 172	53.645	60.728	-16.359	1.00	85.78	A1
ATOM 1324 C LBU 172	54.813	56.357	-17.180	1.00	85.78	A1

FIGURE 5

ATOM 1325 O LEU 172	55.896	36.640	17.692	1.00	86.23	A3	ATOM 1376 CD1 PHE 214	45.176	39.459	23.044	1.00	42.77	H1
ATOM 1326 N LEU 172	55.896	36.640	17.692	1.00	85.49	A3	ATOM 1377 CD2 PHE 214	46.818	37.794	23.400	1.00	42.82	H1
ATOM 1327 H ALA 173	53.856	33.776	15.766	1.00	85.65	A3	ATOM 1378 CD3 PHE 214	45.834	36.398	23.422	1.00	41.92	H1
ATOM 1328 CA ALA 173	51.896	34.497	16.007	1.00	85.65	A3	ATOM 1379 CD4 PHE 214	45.834	36.398	23.422	1.00	41.92	H1
ATOM 1329 CB ALA 173	56.602	34.559	14.809	1.00	85.01	A3	ATOM 1380 CF PHE 214	44.519	37.377	23.791	1.00	41.05	H1
ATOM 1330 CG ALA 173	56.602	34.559	14.809	1.00	85.01	A3	ATOM 1381 G PHE 214	47.109	39.656	20.311	1.00	36.54	H1
ATOM 1331 OTT ALA 173	55.896	33.747	16.911	1.00	87.21	A3	ATOM 1382 G PHE 214	47.109	39.656	20.311	1.00	36.54	H1
ATOM 1332 OTT ALA 173	54.650	31.767	15.036	1.00	87.21	A3	ATOM 1383 N LEU 215	46.616	40.812	19.893	1.00	33.27	H1
ATOM 1333 CD1 LEU 210	42.524	42.991	25.453	1.00	51.47	H1	ATOM 1384 H LEU 215	47.008	41.642	20.248	1.00	0.00	H1
ATOM 1334 CD2 LEU 210	42.524	42.991	25.453	1.00	51.47	H1	ATOM 1385 I LEU 215	45.585	40.812	19.893	1.00	33.27	H1
ATOM 1335 CD3 LEU 210	42.524	42.991	25.453	1.00	51.47	H1	ATOM 1386 C LEU 215	45.099	41.382	18.708	1.00	29.48	H1
ATOM 1336 CD4 LEU 210	42.524	42.991	25.453	1.00	51.47	H1	ATOM 1387 CG LEU 215	43.857	42.530	17.893	1.00	31.78	H1
ATOM 1337 CD5 LEU 210	42.524	42.991	25.453	1.00	51.47	H1	ATOM 1388 CD LEU 215	43.857	42.530	17.893	1.00	31.78	H1
ATOM 1338 O LEU 210	46.475	45.167	23.796	1.00	31.76	H1	ATOM 1389 CD LEU 215	47.272	41.963	18.737	1.00	31.95	H1
ATOM 1339 HT1 LEU 210	46.475	45.167	23.796	1.00	31.76	H1	ATOM 1390 CD LEU 215	45.811	40.232	17.648	1.00	29.57	H1
ATOM 1340 HT2 LEU 210	45.157	45.974	25.414	1.00	0.00	H1	ATOM 1391 O LEU 215	44.932	39.632	17.055	1.00	31.48	H1
ATOM 1341 HT3 LEU 210	45.157	45.974	25.414	1.00	0.00	H1	ATOM 1392 I LEU 216	47.657	40.335	17.719	1.00	35.44	H1
ATOM 1342 HT4 LEU 210	43.855	45.012	25.997	1.00	0.00	H1	ATOM 1393 H LEU 216	47.657	40.335	17.719	1.00	35.44	H1
ATOM 1343 CA LEU 210	45.730	44.028	25.676	1.00	52.35	H1	ATOM 1394 CA LEU 216	47.465	39.790	15.893	1.00	29.89	H1
ATOM 1344 CB LEU 211	45.730	44.028	25.676	1.00	52.35	H1	ATOM 1395 CD LEU 216	48.781	40.450	15.472	1.00	26.61	H1
ATOM 1345 CD LEU 211	45.730	44.028	25.676	1.00	52.35	H1	ATOM 1396 CD LEU 216	48.781	40.450	15.472	1.00	26.61	H1
ATOM 1346 CA PRO 211	48.895	44.911	23.419	1.00	49.04	H1	ATOM 1397 CD LEU 216	48.781	40.450	15.472	1.00	26.61	H1
ATOM 1347 CB PRO 211	48.895	44.911	23.419	1.00	49.04	H1	ATOM 1398 CD LEU 216	48.781	40.450	15.472	1.00	26.61	H1
ATOM 1348 CD PRO 211	48.895	44.911	23.419	1.00	49.04	H1	ATOM 1399 CD LEU 216	48.781	40.450	15.472	1.00	26.61	H1
ATOM 1349 O PRO 211	48.544	43.864	21.965	1.00	48.03	H1	ATOM 1400 O LEU 216	48.544	43.864	21.965	1.00	48.03	H1
ATOM 1350 O PRO 211	48.544	43.864	21.965	1.00	48.03	H1	ATOM 1401 N LYS 217	47.999	37.816	17.261	1.00	31.50	H1
ATOM 1351 N GLN 212	47.872	42.896	21.623	1.00	49.05	H1	ATOM 1402 I LYS 217	48.305	38.432	17.936	1.00	0.00	H1
ATOM 1352 N GLN 212	47.872	42.896	21.623	1.00	49.05	H1	ATOM 1403 I LYS 217	48.305	38.432	17.936	1.00	0.00	H1
ATOM 1353 CA GLN 212	48.839	44.461	19.641	1.00	45.47	H1	ATOM 1404 CB LYS 217	48.645	36.860	19.002	1.00	38.07	H1
ATOM 1354 CB GLN 212	48.839	44.461	19.641	1.00	45.47	H1	ATOM 1405 CG LYS 217	49.394	34.378	19.109	1.00	45.25	H1
ATOM 1355 CD GLN 212	48.839	44.461	19.641	1.00	45.47	H1	ATOM 1406 CG LYS 217	49.394	34.378	19.109	1.00	45.25	H1
ATOM 1356 CD GLN 212	48.839	44.461	19.641	1.00	45.47	H1	ATOM 1407 CE LYS 217	50.213	32.155	21.467	1.00	66.10	H1
ATOM 1357 OE GLN 212	48.489	47.673	16.232	1.00	57.72	H1	ATOM 1408 NE LYS 217	50.213	32.155	21.467	1.00	66.10	H1
ATOM 1358 NE GLN 212	50.086	46.176	16.074	1.00	52.39	H1	ATOM 1409 NE LYS 217	49.239	32.054	21.824	1.00	0.00	H1
ATOM 1359 O GLN 212	50.086	46.176	16.074	1.00	52.39	H1	ATOM 1410 NE LYS 217	49.239	32.054	21.824	1.00	0.00	H1
ATOM 1360 NE2 GLN 212	50.341	46.675	16.244	1.00	0.00	H1	ATOM 1411 NE2 LYS 217	50.584	31.985	21.179	1.00	0.00	H1
ATOM 1361 C GLN 212	49.390	43.133	19.185	1.00	44.79	H1	ATOM 1412 C LYS 217	46.617	35.950	17.546	1.00	36.77	H1
ATOM 1362 C GLN 212	49.390	43.133	19.185	1.00	44.79	H1	ATOM 1413 C LYS 217	46.617	35.950	17.546	1.00	36.77	H1
ATOM 1363 N SER 213	50.907	43.115	19.008	1.00	44.79	H1	ATOM 1414 C LYS 217	46.617	35.950	17.546	1.00	36.77	H1
ATOM 1364 H SER 213	50.907	43.115	19.008	1.00	44.79	H1	ATOM 1415 H CYS 218	45.907	37.388	18.751	1.00	0.00	H1
ATOM 1365 CA SER 213	51.025	41.424	19.321	1.00	41.76	H1	ATOM 1416 CA CYS 218	44.277	38.218	18.076	1.00	33.63	H1
ATOM 1366 CB SER 213	51.025	41.424	19.321	1.00	41.76	H1	ATOM 1417 CB CYS 218	44.277	38.218	18.076	1.00	33.63	H1
ATOM 1367 CG SER 213	51.025	41.424	19.321	1.00	41.76	H1	ATOM 1418 CG CYS 218	44.277	38.218	18.076	1.00	33.63	H1
ATOM 1368 HG SER 213	51.025	41.424	19.321	1.00	41.76	H1	ATOM 1419 C CYS 218	43.766	36.189	16.652	1.00	31.87	H1
ATOM 1369 O SER 213	49.984	39.492	18.947	1.00	41.32	H1	ATOM 1420 C CYS 218	43.766	36.189	16.652	1.00	31.87	H1
ATOM 1370 O SER 213	49.984	39.492	18.947	1.00	41.32	H1	ATOM 1421 N LEU 219	44.035	37.165	15.773	1.00	29.57	H1
ATOM 1371 N PHE 214	49.245	40.571	20.876	1.00	38.86	H1	ATOM 1422 H LEU 219	43.814	37.960	16.104	1.00	0.00	H1
ATOM 1372 H PHE 214	49.245	40.571	20.876	1.00	38.86	H1	ATOM 1423 CA ILE 219	43.814	37.960	16.104	1.00	0.00	H1
ATOM 1373 CA ILE 219	49.245	40.571	20.876	1.00	38.86	H1	ATOM 1424 CA ILE 219	43.814	37.960	16.104	1.00	0.00	H1
ATOM 1374 CB PHE 214	47.568	40.964	21.631	1.00	31.45	H1	ATOM 1425 CG ILE 219	43.814	37.960	16.104	1.00	0.00	H1
ATOM 1375 CG PHE 214	46.494	39.980	23.035	1.00	41.31	H1	ATOM 1426 CD ILE 219	42.402	38.975	11.796	1.00	36.24	H1

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1428	C	CRU	LB2	219	44,563	40,01	11,882	100,22,10	BI	ATOM	1478	II	CVS	224	42,720	37,123	10,594	1,009,000	BI
1429	C	CRU	LB2	219	44,121	35,867	16,634	1,000,28,24	BI	ATOM	1479	II	CVS	224	42,720	37,123	10,594	1,009,000	BI
1430	C	CRU	LB2	219	44,121	35,867	16,634	1,000,28,24	BI	ATOM	1480	II	CVS	224	42,720	37,123	10,594	1,009,000	BI
1431	C	CRU	LB2	219	44,563	35,974	14,448	1,000,0,00	BI	ATOM	1481	II	CVS	224	42,720	37,123	10,594	1,009,000	BI
1432	C	CRU	LB2	219	44,563	34,411	13,048	1,000,28,18	BI	ATOM	1482	II	CVS	224	42,720	37,123	10,594	1,009,000	BI
1433	C	CRU	LB2	219	44,563	34,411	13,048	1,000,28,18	BI	ATOM	1483	II	CVS	224	42,720	37,123	10,594	1,009,000	BI
1434	C	CRU	LB2	219	44,563	34,411	13,048	1,000,28,18	BI	ATOM	1484	II	CVS	224	42,720	37,123	10,594	1,009,000	BI
1435	C	CRU	LB2	219	44,563	34,411	13,048	1,000,28,18	BI	ATOM	1485	II	CVS	224	42,720	37,123	10,594	1,009,000	BI
1436	C	CRU	LB2	219	44,563	34,411	13,048	1,000,28,18	BI	ATOM	1486	II	CVS	224	42,720	37,123	10,594	1,009,000	BI
1437	C	CRU	LB2	219	44,563	34,411	13,048	1,000,28,18	BI	ATOM	1487	II	CVS	224	42,720	37,123	10,594	1,009,000	BI
1438	C	CRU	LB2	219	44,563	34,411	13,048	1,000,28,18	BI	ATOM	1488	II	CVS	224	42,720	37,123	10,594	1,009,000	BI
1439	C	CRU	LB2	219	44,563	34,411	13,048	1,000,28,18	BI	ATOM	1489	II	CVS	224	42,720	37,123	10,594	1,009,000	BI
1440	C	CRU	LB2	219	44,563	34,411	13,048	1,000,28,18	BI	ATOM	1490	II	CVS	224	42,720	37,123	10,594	1,009,000	BI
1441	C	CRU	LB2	219	44,563	34,411	13,048	1,000,28,18	BI	ATOM	1491	II	CVS	224	42,720	37,123	10,594	1,009,000	BI
1442	C	CRU	LB2	219	44,563	34,411	13,048	1,000,28,18	BI	ATOM	1492	II	CVS	224	42,720	37,123	10,594	1,009,000	BI
1443	C	CRU	LB2	219	44,563	34,411	13,048	1,000,28,18	BI	ATOM	1493	II	CVS	224	42,720	37,123	10,594	1,009,000	BI
1444	C	CRU	LB2	219	44,563	34,411	13,048	1,000,28,18	BI	ATOM	1494	II	CVS	224	42,720	37,123	10,594	1,009,000	BI
1445	C	CRU	LB2	219	44,563	34,411	13,048	1,000,28,18	BI	ATOM	1495	II	CVS	224	42,720	37,123	10,594	1,009,000	BI
1446	C	CRU	LB2	219	44,563	34,411	13,048	1,000,28,18	BI	ATOM	1496	II	CVS	224	42,720	37,123	10,594	1,009,000	BI
1447	C	CRU	LB2	219	44,563	34,411	13,048	1,000,28,18	BI	ATOM	1497	II	CVS	224	42,720	37,123	10,594	1,009,000	BI
1448	C	CRU	LB2	219	44,563	34,411	13,048	1,000,28,18	BI	ATOM	1498	II	CVS	224	42,720	37,123	10,594	1,009,000	BI
1449	C	CRU	LB2	219	44,563	34,411	13,048	1,000,28,18	BI	ATOM	1499	II	CVS	224	42,720	37,123	10,594	1,009,000	BI
1450	C	CRU	LB2	219	44,563	34,411	13,048	1,000,28,18	BI	ATOM	1500	II	CVS	224	42,720	37,123	10,594	1,009,000	BI
1451	C	CRU	LB2	219	44,563	34,411	13,048	1,000,28,18	BI	ATOM	1501	II	CVS	224	42,720	37,123	10,594	1,009,000	BI
1452	C	CRU	LB2	219	44,563	34,411	13,048	1,000,28,18	BI	ATOM	1502	II	CVS	224	42,720	37,123	10,594	1,009,000	BI
1453	C	CRU	LB2	219	44,563	34,411	13,048	1,000,28,18	BI	ATOM	1503	II	CVS	224	42,720	37,123	10,594	1,009,000	BI
1454	C	CRU	LB2	219	44,563	34,411	13,048	1,000,28,18	BI	ATOM	1504	II	CVS	224	42,720	37,123	10,594	1,009,000	BI
1455	C	CRU	LB2	219	44,563	34,411	13,048	1,000,28,18	BI	ATOM	1505	II	CVS	224	42,720	37,123	10,594	1,009,000	BI
1456	C	CRU	LB2	219	44,563	34,411	13,048	1,000,28,18	BI	ATOM	1506	II	CVS	224	42,720	37,123	10,594	1,009,000	BI
1457	C	CRU	LB2	219	44,563	34,411	13,048	1,000,28,18	BI	ATOM	1507	II	CVS	224	42,720	37,123	10,594	1,009,000	BI
1458	C	CRU	LB2	219	44,563	34,411	13,048	1,000,28,18	BI	ATOM	1508	II	CVS	224	42,720	37,123	10,594	1,009,000	BI
1459	C	CRU	LB2	219	44,563	34,411	13,048	1,000,28,18	BI	ATOM	1509	II	CVS	224	42,720	37,123	10,594	1,009,000	BI
1460	C	CRU	LB2	219	44,563	34,411	13,048	1,000,28,18	BI	ATOM	1510	II	CVS	224	42,720	37,123	10,594	1,009,000	BI
1461	C	CRU	LB2	219	44,563	34,411	13,048	1,000,28,18	BI	ATOM	1511	II	CVS	224	42,720	37,123	10,594	1,009,000	BI
1462	C	CRU	LB2	219	44,563	34,411	13,048	1,000,28,18	BI	ATOM	1512	II	CVS	224	42,720	37,123	10,594	1,009,000	BI
1463	C	CRU	LB2	219	44,563	34,411	13,048	1,000,28,18	BI	ATOM	1513	II	CVS	224	42,720	37,123	10,594	1,009,000	BI
1464	C	CRU	LB2	219	44,563	34,411	13,048	1,000,28,18	BI	ATOM	1514	II	CVS	224	42,720	37,123	10,594	1,009,000	BI
1465	C	CRU	LB2	219	44,563	34,411	13,048	1,000,28,18	BI	ATOM	1515	II	CVS	224	42,720	37,123	10,594	1,009,000	BI
1466	C	CRU	LB2	219	44,563	34,411	13,048	1,000,28,18	BI	ATOM	1516	II	CVS	224	42,720	37,123	10,594	1,009,000	BI
1467	C	CRU	LB2	219	44,563	34,411	13,048	1,000,28,18	BI	ATOM	1517	II	CVS	224	42,720	37,123	10,594	1,009,000	BI
1468	C	CRU	LB2	219	44,563	34,411	13,048	1,000,28,18	BI	ATOM	1518	II	CVS	224	42,720	37,123	10,594	1,009,000	BI
1469	C	CRU	LB2	219	44,563	34,411	13,048	1,000,28,18	BI	ATOM	1519	II	CVS	224	42,720	37,123	10,594	1,009,000	BI
1470	C	CRU	LB2	219	44,563	34,411	13,048	1,000,28,18	BI	ATOM	1520	II	CVS	224	42,720	37,123	10,594	1,009,000	BI
1471	C	CRU	LB2	219	44,563	34,411	13,048	1,000,28,18	BI	ATOM	1521	II	CVS	224	42,720	37,123	10,594	1,009,000	BI
1472	C	CRU	LB2	219	44,563	34,411	13,048	1,000,28,18	BI	ATOM	1522	II	CVS	224	42,720	37,123	10,594	1,009,000	BI
1473	C	CRU	LB2	219	44,563	34,411	13,048	1,000,28,18	BI	ATOM	1523	II	CVS	224	42,720	37,123	10,594	1,009,000	BI
1474	C	CRU	LB2	219	44,563	34,411	13,048	1,000,28,18	BI	ATOM	1524	II	CVS	224	42,720	37,123	10,594	1,009,000	BI
1475	C	CRU	LB2	219	44,563	34,411	13,048	1,000,28,18	BI	ATOM	1525	II	CVS	224	42,720	37,123	10,594	1,009,000	BI
1476	C	CRU	LB2	219	44,563	34,411	13,048	1,000,28,18	BI	ATOM	1526	II	CVS	224	42,720	37,123	10,594	1,009,000	BI
1477	C	CRU	LB2	219	44,563	34,411	13,048	1,000,28,18	BI	ATOM	1527	II	CVS	224	42,720	37,123	10,594	1,009,000	BI
1478	C	CRU	LB2	219	44,563	34,411	13,048	1,000,28,18	BI	ATOM	1528	II	CVS	224	42,720	37,123	10,594	1,009,000	BI

FIGURE 5

ATOM	1631	N	LVS	241	24.174	18.011	0.694	1.00	37.36	81
ATOM	1632	N	LVS	241	22.091	18.021	0.345	1.00	37.46	81
ATOM	1633	N	LVS	241	22.091	18.021	0.345	1.00	37.46	81
ATOM	1634	CS	LVS	241	21.713	18.046	-0.595	1.00	18.18	81
ATOM	1635	CS	LVS	241	22.645	17.940	-1.838	1.00	42.94	81
ATOM	1636	CS	LVS	241	22.645	17.940	-1.838	1.00	42.94	81
ATOM	1637	N	LVS	241	22.657	18.070	-0.070	1.00	46.97	81
ATOM	1638	N	LVS	241	22.657	18.070	-0.070	1.00	46.97	81
ATOM	1639	N	LVS	241	22.657	18.070	-0.070	1.00	46.97	81
ATOM	1640	N	LVS	241	22.657	18.070	-0.070	1.00	46.97	81
ATOM	1641	HE2	LVS	241	22.447	19.500	-0.518	1.00	0.00	81
ATOM	1642	HE2	LVS	241	22.447	19.500	-0.518	1.00	0.00	81
ATOM	1643	HE2	LVS	241	22.447	19.500	-0.518	1.00	0.00	81
ATOM	1644	N	LVS	241	22.609	17.495	-3.811	1.00	0.00	81
ATOM	1645	N	LVS	241	22.609	17.495	-3.811	1.00	0.00	81
ATOM	1646	N	LVS	241	22.609	17.495	-3.811	1.00	0.00	81
ATOM	1647	N	LVS	241	22.609	17.495	-3.811	1.00	0.00	81
ATOM	1648	CS	LEU	242	22.310	18.814	1.718	1.00	79.62	81
ATOM	1649	CS	LEU	242	22.310	18.814	1.718	1.00	79.62	81
ATOM	1650	N	LEU	242	22.378	19.331	3.550	1.00	34.03	81
ATOM	1651	N	LEU	242	22.378	19.331	3.550	1.00	34.03	81
ATOM	1652	N	LEU	242	22.378	19.331	3.550	1.00	34.03	81
ATOM	1653	N	LEU	242	22.378	19.331	3.550	1.00	34.03	81
ATOM	1654	N	LEU	242	22.378	19.331	3.550	1.00	34.03	81
ATOM	1655	N	LEU	242	22.378	19.331	3.550	1.00	34.03	81
ATOM	1656	N	LEU	242	22.378	19.331	3.550	1.00	34.03	81
ATOM	1657	N	LEU	242	22.378	19.331	3.550	1.00	34.03	81
ATOM	1658	N	LEU	242	22.378	19.331	3.550	1.00	34.03	81
ATOM	1659	N	LEU	242	22.378	19.331	3.550	1.00	34.03	81
ATOM	1660	N	LEU	242	22.378	19.331	3.550	1.00	34.03	81
ATOM	1661	N	LEU	242	22.378	19.331	3.550	1.00	34.03	81
ATOM	1662	N	LEU	242	22.378	19.331	3.550	1.00	34.03	81
ATOM	1663	N	LEU	242	22.378	19.331	3.550	1.00	34.03	81
ATOM	1664	N	LEU	242	22.378	19.331	3.550	1.00	34.03	81
ATOM	1665	CS	HE2	244	20.188	16.584	0.814	1.00	32.79	81
ATOM	1666	CS	HE2	244	20.188	16.584	0.814	1.00	32.79	81
ATOM	1667	N	HE2	244	22.344	18.312	1.778	1.00	40.05	81
ATOM	1668	N	HE2	244	22.344	18.312	1.778	1.00	40.05	81
ATOM	1669	HE2	HE2	244	21.874	17.407	-0.013	1.00	35.95	81
ATOM	1670	N	HE2	244	20.910	16.920	-0.301	1.00	35.54	81
ATOM	1671	N	HE2	244	20.910	16.920	-0.301	1.00	35.54	81
ATOM	1672	N	HE2	244	21.621	16.355	0.609	1.00	33.13	81
ATOM	1673	N	HE2	244	20.546	16.105	0.505	1.00	33.32	81
ATOM	1674	CS	PRO	245	22.833	17.949	-1.000	1.00	34.16	81
ATOM	1675	CS	PRO	245	22.833	17.949	-1.000	1.00	34.16	81
ATOM	1676	N	PRO	245	22.373	16.979	-0.948	1.00	31.79	81
ATOM	1677	N	PRO	245	22.373	16.979	-0.948	1.00	31.79	81
ATOM	1678	N	PRO	245	22.373	16.979	-0.948	1.00	31.79	81
ATOM	1679	N	PRO	245	22.373	16.979	-0.948	1.00	31.79	81
ATOM	1680	N	PRO	245	22.373	16.979	-0.948	1.00	31.79	81
ATOM	1681	N	PRO	245	22.373	16.979	-0.948	1.00	31.79	81
ATOM	1682	CS	GLU	246	19.044	15.729	0.731	1.00	41.15	81
ATOM	1683	CS	GLU	246	19.044	15.729	0.731	1.00	41.15	81
ATOM	1684	CS	GLU	246	20.156	16.018	0.594	1.00	42.07	81
ATOM	1685	CS	GLU	246	20.156	16.018	0.594	1.00	42.07	81
ATOM	1686	CS	GLU	246	22.054	16.045	1.344	1.00	42.41	81
ATOM	1687	CS	GLU	246	22.054	16.045	1.344	1.00	42.41	81
ATOM	1688	CS	GLU	246	20.002	16.259	0.656	1.00	44.57	81
ATOM	1689	CS	GLU	246	20.002	16.259	0.656	1.00	44.57	81
ATOM	1690	N	GLU	247	17.300	13.751	1.001	1.00	48.57	81
ATOM	1691	N	GLU	247	17.300	13.751	1.001	1.00	48.57	81
ATOM	1692	N	GLU	247	15.025	12.388	0.640	1.00	46.32	81
ATOM	1693	N	GLU	247	15.025	12.388	0.640	1.00	46.32	81
ATOM	1694	N	GLU	247	17.750	12.714	0.640	1.00	46.32	81
ATOM	1695	N	GLU	247	17.750	12.714	0.640	1.00	46.32	81
ATOM	1696	N	GLU	247	17.139	15.423	0.642	1.00	46.34	81
ATOM	1697	N	GLU	247	17.139	15.423	0.642	1.00	46.34	81
ATOM	1698	N	GLU	247	16.870	14.960	0.642	1.00	46.34	81
ATOM	1699	N	GLU	247	16.870	14.960	0.642	1.00	46.34	81
ATOM	1700	N	GLU	248	18.046	15.316	0.516	1.00	43.95	81
ATOM	1701	N	GLU	248	18.046	15.316	0.516	1.00	43.95	81
ATOM	1702	N	GLU	248	15.005	13.280	0.760	1.00	37.92	81
ATOM	1703	CS	LEU	248	19.458	13.623	0.976	1.00	34.13	81
ATOM	1704	CS	LEU	248	19.458	13.623	0.976	1.00	34.13	81
ATOM	1705	CS	LEU	248	18.620	13.100	0.322	1.00	32.55	81
ATOM	1706	CS	LEU	248	18.620	13.100	0.322	1.00	32.55	81
ATOM	1707	N	LEU	248	17.471	15.031	1.153	1.00	36.51	81
ATOM	1708	N	LEU	248	17.471	15.031	1.153	1.00	36.51	81
ATOM	1709	N	LEU	248	17.663	15.146	1.046	1.00	36.88	81
ATOM	1710	N	LEU	249	17.566	16.410	0.283	1.00	40.18	81
ATOM	1711	N	LEU	249	17.566	16.410	0.283	1.00	40.18	81
ATOM	1712	N	LEU	249	17.663	16.410	0.283	1.00	40.18	81
ATOM	1713	CS	VAL	249	15.804	12.985	1.176	1.00	43.70	81
ATOM	1714	CS	VAL	249	15.804	12.985	1.176	1.00	43.70	81
ATOM	1715	CS	VAL	249	16.590	13.270	1.044	1.00	45.20	81
ATOM	1716	N	VAL	249	16.912	16.154	0.594	1.00	44.77	81
ATOM	1717	N	VAL	249	16.912	16.154	0.594	1.00	44.77	81
ATOM	1718	N	VAL	249	15.525	16.035	0.194	1.00	41.61	81
ATOM	1719	N	VAL	249	15.525	16.035	0.194	1.00	41.61	81
ATOM	1720	CS	LEU	250	14.107	15.396	1.337	1.00	41.98	81
ATOM	1721	CS	LEU	250	14.107	15.396	1.337	1.00	41.98	81
ATOM	1722	CS	LEU	250	13.092	15.372	1.044	1.00	42.16	81
ATOM	1723	CS	LEU	250	13.092	15.372	1.044	1.00	42.16	81
ATOM	1724	N	LEU	250	12.886	16.772	12.881	1.00	46.16	81
ATOM	1725	N	LEU	250	12.886	16.772	12.881	1.00	46.16	81
ATOM	1726	N	LEU	251	15.691	15.767	0.526	1.00	41.56	81
ATOM	1727	N	LEU	251	15.691	15.767	0.526	1.00	41.56	81
ATOM	1728	N	LEU	251	15.691	15.767	0.526	1.00	41.56	81
ATOM	1729	N	LEU	251	15.691	15.767	0.526	1.00	41.56	81
ATOM	1730	CS	HE2	251	16.834	11.188	14.257	1.00	46.77	81
ATOM	1731	CS	HE2	251	16.834	11.188	14.257	1.00	46.77	81
ATOM	1732	CS	HE2	251	15.996	10.979	12.767	1.00	43.34	81
ATOM	1733	CS	HE2	251	15.996	10.979	12.767	1.00	43.34	81
ATOM	1734	CS	HE2	251	16.075	10.979	12.767	1.00	43.34	81
ATOM	1735	CS	HE2	251	16.075	10.979	12.767	1.00	43.34	81

FIGURE 5

ATOM 1529 O GLY 230	33.370	15.321	7.054	1.00	35.31	BI
ATOM 1530 N ALA 230	35.053	16.441	7.391	1.00	33.97	BI
ATOM 1531 H ALA 230	37.017	17.026	7.654	1.00	0.00	BI
ATOM 1532 C ALA 230	34.530	16.648	6.961	1.00	15.94	BI
ATOM 1533 N ALA 230	34.794	15.403	5.104	1.00	19.42	BI
ATOM 1534 C ALA 230	34.014	15.061	4.423	1.00	32.07	BI
ATOM 1535 O ALA 230	34.014	15.061	4.423	1.00	32.07	BI
ATOM 1536 H ALA 230	36.551	16.441	7.391	1.00	32.16	BI
ATOM 1537 N ALA 231	36.551	16.441	7.391	1.00	32.16	BI
ATOM 1538 C ALA 231	36.141	12.364	4.957	1.00	31.99	BI
ATOM 1539 C ALA 231	37.489	12.847	5.418	1.00	32.77	BI
ATOM 1540 H ALA 231	35.053	16.441	7.391	1.00	33.97	BI
ATOM 1541 O ALA 231	35.174	12.861	7.384	1.00	0.00	BI
ATOM 1542 N ALA 232	34.662	12.809	6.651	1.00	33.30	BI
ATOM 1543 H ALA 232	35.174	12.861	7.384	1.00	0.00	BI
ATOM 1544 C ALA 232	32.779	12.813	6.216	1.00	34.32	BI
ATOM 1545 C ALA 232	32.410	30.661	9.394	1.00	33.16	BI
ATOM 1546 CG LBU 232	32.191	19.545	9.451	1.00	34.59	BI
ATOM 1547 CD LBU 232	32.191	19.545	9.451	1.00	34.59	BI
ATOM 1548 H LBU 232	32.171	21.819	6.640	1.00	36.45	BI
ATOM 1549 C LBU 232	32.171	21.819	6.640	1.00	36.45	BI
ATOM 1550 O LBU 232	31.703	20.986	5.749	1.00	36.42	BI
ATOM 1551 H LBU 232	32.171	21.819	6.640	1.00	36.45	BI
ATOM 1552 H LBU 232	32.171	21.819	6.640	1.00	36.45	BI
ATOM 1553 CA GUN 233	30.637	32.579	5.933	1.00	40.02	BI
ATOM 1554 CG GUN 233	30.572	32.012	6.162	1.00	41.25	BI
ATOM 1555 CD GUN 233	30.572	32.012	6.162	1.00	41.25	BI
ATOM 1556 CG GUN 233	30.021	16.879	7.983	1.00	55.75	BI
ATOM 1557 OEG GUN 233	30.799	27.810	7.718	1.00	55.93	BI
ATOM 1558 H GUN 233	30.635	32.579	5.933	1.00	40.02	BI
ATOM 1559 HEB GUN 233	28.410	28.144	6.902	1.00	0.00	BI
ATOM 1560 HEB GUN 233	28.410	28.144	6.902	1.00	0.00	BI
ATOM 1561 C GUN 234	32.564	23.750	4.163	1.00	0.00	BI
ATOM 1562 H GUN 234	31.744	23.377	3.716	1.00	39.32	BI
ATOM 1563 N GUN 234	31.155	23.454	1.811	1.00	40.25	BI
ATOM 1564 H GUN 234	33.292	23.028	0.383	1.00	47.69	BI
ATOM 1565 CG GUN 234	34.733	23.026	-0.073	1.00	51.40	BI
ATOM 1566 CD GUN 234	34.733	23.026	-0.073	1.00	51.40	BI
ATOM 1567 H GUN 234	35.588	22.400	0.590	1.00	51.55	BI
ATOM 1568 HEB GUN 234	31.480	21.535	2.136	1.00	37.69	BI
ATOM 1569 HEB GUN 234	31.480	21.535	2.136	1.00	37.69	BI
ATOM 1570 C GUN 234	32.092	20.613	2.986	1.00	37.27	BI
ATOM 1571 C GUN 234	32.092	20.613	2.986	1.00	37.27	BI
ATOM 1572 H GUN 234	32.661	20.965	3.706	1.00	0.00	BI
ATOM 1573 N LYS 235	32.316	18.365	3.997	1.00	44.92	BI
ATOM 1574 H LYS 235	32.316	18.365	3.997	1.00	44.92	BI
ATOM 1575 CG LYS 235	33.978	18.483	4.107	1.00	38.47	BI
ATOM 1576 CD LYS 235	34.762	17.999	2.931	1.00	38.07	BI
ATOM 1577 CG LYS 235	36.179	18.051	3.460	1.00	37.15	BI
ATOM 1578 H LYS 235						BI
ATOM 1579 H LYS 235						BI
ATOM 1580 H LYS 235						BI
ATOM 1581 H LYS 235						BI
ATOM 1582 H LYS 235						BI
ATOM 1583 H LYS 235						BI
ATOM 1584 H LYS 236						BI
ATOM 1585 H LYS 236						BI
ATOM 1586 H LYS 236						BI
ATOM 1587 H LYS 236						BI
ATOM 1588 H LYS 236						BI
ATOM 1589 H LYS 236						BI
ATOM 1590 CG LYS 236						BI
ATOM 1591 CD LYS 236						BI
ATOM 1592 H LYS 236						BI
ATOM 1593 H LYS 236						BI
ATOM 1594 O LYS 236						BI
ATOM 1595 H LYS 236						BI
ATOM 1596 H LYS 236						BI
ATOM 1597 CA LYS 237						BI
ATOM 1598 C LYS 237						BI
ATOM 1599 CA LYS 237						BI
ATOM 1600 CG LYS 237						BI
ATOM 1601 CG LYS 237						BI
ATOM 1602 H LYS 237						BI
ATOM 1603 H LYS 237						BI
ATOM 1604 CA LYS 238						BI
ATOM 1605 CG LYS 238						BI
ATOM 1606 CG LYS 238						BI
ATOM 1607 O LYS 238						BI
ATOM 1608 H LYS 238						BI
ATOM 1609 H LYS 238						BI
ATOM 1610 CA LYS 239						BI
ATOM 1611 CG LYS 239						BI
ATOM 1612 CG LYS 239						BI
ATOM 1613 CG LYS 239						BI
ATOM 1614 CG LYS 239						BI
ATOM 1615 C LYS 239						BI
ATOM 1616 H LYS 239						BI
ATOM 1617 H LYS 240						BI
ATOM 1618 H LYS 240						BI
ATOM 1619 CA LYS 240						BI
ATOM 1620 CG LYS 240						BI
ATOM 1621 CG LYS 240						BI
ATOM 1622 CD LYS 240						BI
ATOM 1623 CD LYS 240						BI
ATOM 1624 CD LYS 240						BI
ATOM 1625 CG LYS 240						BI
ATOM 1626 H LYS 240						BI
ATOM 1627 H LYS 240						BI
ATOM 1628 H LYS 240						BI
ATOM 1629 C LYS 240						BI
ATOM 1630 O LYS 240						BI
ATOM 1631 H LYS 240						BI
ATOM 1632 H LYS 240						BI
ATOM 1633 H LYS 240						BI
ATOM 1634 H LYS 240						BI
ATOM 1635 H LYS 240						BI
ATOM 1636 H LYS 240						BI
ATOM 1637 H LYS 240						BI
ATOM 1638 H LYS 240						BI
ATOM 1639 C LYS 240						BI
ATOM 1640 O LYS 240						BI
ATOM 1641 H LYS 240						BI
ATOM 1642 H LYS 240						BI
ATOM 1643 H LYS 240						BI
ATOM 1644 H LYS 240						BI
ATOM 1645 H LYS 240						BI
ATOM 1646 H LYS 240						BI
ATOM 1647 H LYS 240						BI
ATOM 1648 H LYS 240						BI
ATOM 1649 H LYS 240						BI
ATOM 1650 O LYS 240						BI
ATOM 1651 H LYS 240						BI
ATOM 1652 H LYS 240						BI
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ATOM 1670 O LYS 240						BI
ATOM 1671 H LYS 240						BI
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ATOM 1680 O LYS 240						BI
ATOM 1681 H LYS 240						BI
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ATOM 1739 H LYS 240						BI
ATOM 1740 O LYS 240						BI
ATOM 1741 H LYS 240						BI
ATOM 1742 H LYS 240						BI
ATOM 1743 H LYS 240						BI
ATOM 1744 H LYS 240						BI
ATOM 1745 H LYS 240						BI
ATOM 1746 H LYS 240						BI
ATOM 1747 H LYS 240						BI
ATOM 1748 H LYS 240						

FIGURE 5

ATOM 1733 C LEU 251	17100	22.375	15.493	1.00	42.78	BI
ATOM 1734 O LEU 251	17124	22.574	16.395	1.00	45.44	BI
ATOM 1735 N LEU 251	17127	16.935	1.00	44.46	BI	
ATOM 1736 H GLY 252	17150	24.160	14.910	1.00	0.00	BI
ATOM 1737 CA LEU 252	18.134	23.711	16.719	1.00	46.68	BI
ATOM 1738 C LEU 252	18.134	23.711	16.719	1.00	46.68	BI
ATOM 1739 N LEU 252	18.099	22.316	16.027	1.00	40.13	BI
ATOM 1740 N HIS 253	16.756	22.387	18.046	1.00	51.74	BI
ATOM 1741 H HIS 253	16.358	24.055	17.890	1.00	0.00	BI
ATOM 1742 CD LEU 253	12.011	24.529	19.414	1.00	71.00	BI
ATOM 1743 C LEU 253	13.312	23.813	19.537	1.00	68.75	BI
ATOM 1744 CG HIS 253	14.468	24.157	18.764	1.00	62.99	BI
ATOM 1745 CD LEU 253	11.156	23.973	20.104	1.00	71.91	BI
ATOM 1746 NEZ HIS 253	11.156	23.973	20.104	1.00	71.91	BI
ATOM 1747 HDI HIS 253	13.627	22.193	20.810	1.00	70.67	BI
ATOM 1748 CEI HIS 253	11.723	22.966	20.845	1.00	70.00	BI
ATOM 1749 NEZ HIS 253	11.156	23.973	20.104	1.00	71.91	BI
ATOM 1750 N SER 254	15.840	21.827	20.857	1.00	56.17	BI
ATOM 1751 C SER 254	15.840	21.827	20.857	1.00	56.06	BI
ATOM 1752 H SER 254	15.392	21.251	17.814	1.00	54.06	BI
ATOM 1753 N SER 254	15.392	21.251	17.814	1.00	54.46	BI
ATOM 1754 C SER 254	14.613	19.595	17.576	1.00	53.46	BI
ATOM 1755 CA SER 254	15.177	20.034	18.898	1.00	52.61	BI
ATOM 1756 C SER 254	14.613	19.595	17.576	1.00	53.61	BI
ATOM 1757 H SER 254	15.149	20.487	18.119	1.00	51.00	BI
ATOM 1758 H SER 254	15.149	20.487	18.119	1.00	51.00	BI
ATOM 1759 C SER 254	16.512	19.386	19.235	1.00	51.48	BI
ATOM 1760 O SER 254	16.596	18.639	20.245	1.00	51.90	BI
ATOM 1761 H LEU 255	17.410	20.480	17.889	1.00	0.00	BI
ATOM 1762 CA LEU 255	18.513	19.272	18.723	1.00	46.02	BI
ATOM 1763 C LEU 255	18.513	19.272	18.723	1.00	46.66	BI
ATOM 1764 CD LEU 255	15.305	18.968	16.374	1.00	44.51	BI
ATOM 1765 H LEU 255	15.305	18.968	16.374	1.00	44.16	BI
ATOM 1766 CD LEU 255	19.810	19.679	15.006	1.00	41.16	BI
ATOM 1767 CD LEU 255	19.969	17.604	16.456	1.00	41.16	BI
ATOM 1768 O LEU 255	20.165	19.174	16.440	1.00	46.32	BI
ATOM 1769 O LEU 255	20.165	19.174	16.440	1.00	46.82	BI
ATOM 1770 N GLY 256	18.918	20.759	20.281	1.00	45.93	BI
ATOM 1771 H GLY 256	18.918	20.759	20.281	1.00	45.93	BI
ATOM 1772 C GLY 256	20.669	21.846	22.056	1.00	49.84	BI
ATOM 1773 O GLY 256	21.773	21.844	22.056	1.00	49.84	BI
ATOM 1774 O GLY 256	21.773	21.844	22.056	1.00	49.84	BI
ATOM 1775 N LEU 257	22.481	23.017	20.726	1.00	43.64	BI
ATOM 1776 H LEU 257	22.481	23.017	20.726	1.00	43.64	BI
ATOM 1777 CA LEU 257	22.684	23.363	19.237	1.00	41.54	BI
ATOM 1778 C LEU 257	22.684	23.363	19.237	1.00	41.05	BI
ATOM 1779 N SER 263	22.694	22.088	18.437	1.00	40.55	BI
ATOM 1780 CG HLE 257	22.652	22.446	16.970	1.00	39.49	BI
ATOM 1781 C HLE 257	22.652	22.446	16.970	1.00	39.49	BI
ATOM 1782 H HLE 257	21.106	25.110	21.450	1.00	41.77	BI
ATOM 1783 H HLE 257	21.106	25.110	21.450	1.00	41.77	BI
ATOM 1784 N PRO 258	23.441	24.392	21.608	1.00	41.05	BI
ATOM 1785 CD PRO 258	23.441	24.392	21.608	1.00	41.05	BI
ATOM 1786 C PRO 258	23.441	24.392	21.608	1.00	41.05	BI
ATOM 1787 CG PRO 258	24.295	25.216	24.612	1.00	41.97	BI
ATOM 1788 CG PRO 258	25.107	24.064	24.186	1.00	42.79	BI
ATOM 1789 H PRO 258	24.981	26.513	21.556	1.00	46.75	BI
ATOM 1790 O PRO 258	24.981	26.513	21.556	1.00	46.75	BI
ATOM 1791 N TRP 259	23.996	27.887	21.106	1.00	41.45	BI
ATOM 1792 H TRP 259	23.580	27.931	21.954	1.00	0.00	BI
ATOM 1793 CD TRP 259	23.580	27.931	21.954	1.00	0.00	BI
ATOM 1794 C TRP 259	23.580	27.931	21.954	1.00	0.00	BI
ATOM 1795 CG TRP 259	23.556	31.372	21.749	1.00	47.51	BI
ATOM 1796 CD TRP 259	23.860	31.525	20.430	1.00	47.81	BI
ATOM 1797 CEZ TRP 259	24.013	31.421	21.618	1.00	48.27	BI
ATOM 1798 CEI TRP 259	23.639	32.520	22.493	1.00	48.60	BI
ATOM 1799 CD TRP 259	23.639	32.520	22.493	1.00	48.60	BI
ATOM 1800 NEI TRP 259	24.013	31.421	21.618	1.00	48.27	BI
ATOM 1801 NEI TRP 259	24.226	34.344	21.820	1.00	48.87	BI
ATOM 1802 NEI TRP 259	24.226	34.344	21.820	1.00	48.87	BI
ATOM 1803 NEI TRP 259	24.226	34.344	21.820	1.00	48.87	BI
ATOM 1804 CH2 TRP 259	24.613	31.706	18.050	1.00	49.12	BI
ATOM 1805 C TRP 259	25.459	37.217	21.440	1.00	44.01	BI
ATOM 1806 O TRP 259	25.459	37.217	21.440	1.00	44.01	BI
ATOM 1807 N ALA 260	26.409	30.242	21.797	1.00	43.01	BI
ATOM 1808 H ALA 260	26.409	30.242	21.797	1.00	43.01	BI
ATOM 1809 CA ALA 260	27.493	30.874	24.671	1.00	41.25	BI
ATOM 1810 C ALA 260	27.493	30.874	24.671	1.00	41.25	BI
ATOM 1811 C ALA 260	27.493	30.874	24.671	1.00	41.25	BI
ATOM 1812 O ALA 260	27.315	31.946	22.054	1.00	40.55	BI
ATOM 1813 N PRO 261	26.853	33.367	24.253	1.00	40.55	BI
ATOM 1814 CD PRO 261	26.527	32.807	25.606	1.00	41.33	BI
ATOM 1815 C PRO 261	26.527	32.807	25.606	1.00	41.33	BI
ATOM 1816 CG PRO 261	25.778	34.987	25.335	1.00	41.46	BI
ATOM 1817 CG PRO 261	26.251	34.060	26.411	1.00	40.10	BI
ATOM 1818 C PRO 261	26.087	35.369	25.011	1.00	42.27	BI
ATOM 1819 O PRO 261	26.087	35.369	25.011	1.00	42.27	BI
ATOM 1820 N LEU 262	28.234	36.403	21.486	1.00	45.20	BI
ATOM 1821 LEU 262	27.513	36.610	22.853	1.00	0.00	BI
ATOM 1822 CA LEU 262	27.513	36.610	22.853	1.00	0.00	BI
ATOM 1823 C LEU 262	26.531	36.609	22.610	1.00	45.07	BI
ATOM 1824 CG LEU 262	31.903	37.157	21.964	1.00	41.55	BI
ATOM 1825 CD LEU 262	32.344	36.695	24.338	1.00	41.52	BI
ATOM 1826 O LEU 262	32.344	36.695	24.338	1.00	41.52	BI
ATOM 1827 C LEU 262	29.154	38.618	23.015	1.00	48.36	BI
ATOM 1828 O LEU 262	29.633	39.470	21.790	1.00	48.23	BI
ATOM 1829 H SER 263	27.385	40.511	20.612	1.00	51.17	BI
ATOM 1830 H SER 263	27.385	40.511	20.612	1.00	51.17	BI
ATOM 1831 CA SER 263	27.987	40.319	21.494	1.00	55.19	BI
ATOM 1832 C SER 263	26.871	40.511	20.612	1.00	51.17	BI
ATOM 1833 C SER 263	26.871	40.511	20.612	1.00	51.17	BI
ATOM 1834 HLE SER 263	26.091	38.741	20.336	1.00	0.00	BI

FIGURE 5

ATOM 1937 H C1V 282	33.043	31.058	36.221	1.00	0.00	B2
ATOM 1937 H C1V 283	31.735	28.937	33.755	1.00	39.06	B2
ATOM 1939 C C1V 282	32.384	28.075	33.107	1.00	00.10	B2
ATOM 1940 O C1V 282	32.584	28.075	33.107	1.00	00.10	B2
ATOM 1941 H C1V 283	34.380	31.213	34.380	1.00	39.39	B2
ATOM 1941 H C1V 284	34.380	31.213	34.380	1.00	39.39	B2
ATOM 1943 CA LBU 283	35.465	32.133	33.037	1.00	35.06	B2
ATOM 1944 CB LBU 283	36.907	28.718	33.089	1.00	30.20	B2
ATOM 1944 CB LBU 284	38.359	30.461	32.664	1.00	24.38	B2
ATOM 1946 CD LBU 283	37.036	29.402	30.815	1.00	21.94	B2
ATOM 1947 CD LBU 284	35.470	28.451	28.651	1.00	34.81	B2
ATOM 1948 C LBU 283	35.470	28.451	28.651	1.00	34.81	B2
ATOM 1948 C LBU 284	35.470	28.451	28.651	1.00	34.81	B2
ATOM 1950 N PHE 284	35.533	36.842	34.973	1.00	37.62	B2
ATOM 1951 H PHE 284	35.567	37.686	35.467	1.00	00.00	B2
ATOM 1952 H PHE 284	35.567	37.686	35.467	1.00	00.00	B2
ATOM 1953 CH PHE 284	35.567	37.686	35.467	1.00	00.00	B2
ATOM 1954 CG PHE 284	35.567	37.686	35.467	1.00	00.00	B2
ATOM 1955 CH PHE 284	35.567	37.686	35.467	1.00	00.00	B2
ATOM 1956 CH PHE 284	35.567	37.686	35.467	1.00	00.00	B2
ATOM 1957 CEI PHE 284	35.567	37.686	35.467	1.00	00.00	B2
ATOM 1958 CEI PHE 284	35.567	37.686	35.467	1.00	00.00	B2
ATOM 1959 CEI PHE 284	35.567	37.686	35.467	1.00	00.00	B2
ATOM 1960 CEI PHE 284	35.567	37.686	35.467	1.00	00.00	B2
ATOM 1961 O PHE 284	35.567	37.686	35.467	1.00	00.00	B2
ATOM 1962 N LBU 285	33.100	32.563	32.101	1.00	41.74	B2
ATOM 1963 N LBU 286	33.100	32.563	32.101	1.00	41.74	B2
ATOM 1964 CA LBU 285	31.781	23.025	24.730	1.00	39.05	B2
ATOM 1965 CA LBU 286	30.727	26.139	24.407	1.00	39.05	B2
ATOM 1966 CB LBU 285	28.471	26.981	25.663	1.00	41.12	B2
ATOM 1967 CB LBU 286	28.471	26.981	25.663	1.00	41.12	B2
ATOM 1968 CD LBU 285	28.471	26.981	25.663	1.00	39.60	B2
ATOM 1969 C LBU 285	31.740	25.551	23.329	1.00	35.74	B2
ATOM 1970 C LBU 286	31.740	25.551	23.329	1.00	35.74	B2
ATOM 1971 H TYR 286	32.352	35.172	32.372	1.00	35.36	B2
ATOM 1972 H TYR 286	32.352	35.172	32.372	1.00	35.36	B2
ATOM 1973 H TYR 286	32.352	35.172	32.372	1.00	35.36	B2
ATOM 1974 CH TYR 286	32.352	35.172	32.372	1.00	35.36	B2
ATOM 1975 CG TYR 286	32.352	35.172	32.372	1.00	35.36	B2
ATOM 1976 CH TYR 286	32.352	35.172	32.372	1.00	35.36	B2
ATOM 1977 CG TYR 286	32.352	35.172	32.372	1.00	35.36	B2
ATOM 1978 CD TYR 286	32.352	35.172	32.372	1.00	35.36	B2
ATOM 1979 CE TYR 286	32.352	35.172	32.372	1.00	35.36	B2
ATOM 1980 CE TYR 286	32.352	35.172	32.372	1.00	35.36	B2
ATOM 1981 CH TYR 286	32.352	35.172	32.372	1.00	35.36	B2
ATOM 1982 HH TYR 286	32.352	35.172	32.372	1.00	35.36	B2
ATOM 1983 C TYR 286	32.352	35.172	32.372	1.00	35.36	B2
ATOM 1984 CH TYR 286	32.352	35.172	32.372	1.00	35.36	B2
ATOM 1985 N ALA 287	34.527	32.339	31.836	1.00	34.46	B2
ATOM 1986 H ALA 287	34.527	32.339	31.836	1.00	34.46	B2
ATOM 1987 H ALA 287	34.527	32.339	31.836	1.00	34.46	B2
ATOM 1988 CH ALA 287	34.527	32.339	31.836	1.00	34.46	B2
ATOM 1989 CH ALA 287	34.527	32.339	31.836	1.00	34.46	B2
ATOM 1990 O ALA 287	34.527	32.339	31.836	1.00	34.46	B2
ATOM 1991 N GLY 288	33.723	31.211	31.111	1.00	33.19	B2
ATOM 1992 H GLY 288	33.791	31.985	33.564	1.00	00.00	B2
ATOM 1993 H GLY 288	33.791	31.985	33.564	1.00	00.00	B2
ATOM 1994 C GLY 288	33.744	33.606	32.636	1.00	36.89	B2
ATOM 1995 O GLY 288	33.624	32.379	32.444	1.00	34.97	B2
ATOM 1996 CA LBU 289	30.018	20.749	20.954	1.00	35.05	B2
ATOM 1997 H LBU 289	31.000	21.476	22.201	1.00	00.00	B2
ATOM 1998 CA LBU 289	30.018	20.749	20.954	1.00	35.05	B2
ATOM 1999 C LBU 289	31.515	21.576	20.503	1.00	36.32	B2
ATOM 2000 H LBU 289	31.515	21.576	20.503	1.00	36.32	B2
ATOM 2001 CD LBU 289	31.236	23.321	20.890	1.00	31.68	B2
ATOM 2002 CD LBU 289	31.236	23.321	20.890	1.00	31.68	B2
ATOM 2003 CD LBU 289	31.236	23.321	20.890	1.00	31.68	B2
ATOM 2004 O LBU 289	31.236	23.321	20.890	1.00	31.68	B2
ATOM 2005 N LBU 290	31.236	23.321	20.890	1.00	31.68	B2
ATOM 2006 H LBU 290	31.236	23.321	20.890	1.00	31.68	B2
ATOM 2007 H LBU 290	31.236	23.321	20.890	1.00	31.68	B2
ATOM 2008 CB LBU 290	31.236	23.321	20.890	1.00	31.68	B2
ATOM 2009 CG LBU 290	31.236	23.321	20.890	1.00	31.68	B2
ATOM 2010 CG LBU 290	31.236	23.321	20.890	1.00	31.68	B2
ATOM 2011 CD LBU 290	31.236	23.321	20.890	1.00	31.68	B2
ATOM 2012 C LBU 290	31.236	23.321	20.890	1.00	31.68	B2
ATOM 2013 O LBU 290	31.236	23.321	20.890	1.00	31.68	B2
ATOM 2014 H GLY 291	31.515	21.576	20.503	1.00	36.32	B2
ATOM 2015 N GLY 291	31.515	21.576	20.503	1.00	36.32	B2
ATOM 2016 CA GLY 291	33.499	16.372	20.311	1.00	36.39	B2
ATOM 2017 CB GLY 291	33.499	16.372	20.311	1.00	36.39	B2
ATOM 2018 CG GLY 291	34.936	15.367	21.950	1.00	39.48	B2
ATOM 2019 CD GLY 291	35.658	15.367	21.950	1.00	40.79	B2
ATOM 2020 CE GLY 291	35.658	15.367	21.950	1.00	40.79	B2
ATOM 2021 CH GLY 291	35.658	15.367	21.950	1.00	40.79	B2
ATOM 2022 CH GLY 291	35.658	15.367	21.950	1.00	40.79	B2
ATOM 2023 CH GLY 291	35.658	15.367	21.950	1.00	40.79	B2
ATOM 2024 CH GLY 291	35.658	15.367	21.950	1.00	40.79	B2
ATOM 2025 O GLY 291	35.658	15.367	21.950	1.00	40.79	B2
ATOM 2026 N ALA 292	31.143	16.023	20.913	1.00	38.37	B2
ATOM 2027 H ALA 292	31.143	16.023	20.913	1.00	38.37	B2
ATOM 2028 CA ALA 292	29.778	15.451	20.453	1.00	39.25	B2
ATOM 2029 CB ALA 292	28.818	16.485	21.444	1.00	40.78	B2
ATOM 2030 C ALA 292	29.215	14.999	19.444	1.00	38.65	B2
ATOM 2031 CH ALA 292	29.215	14.999	19.444	1.00	38.65	B2
ATOM 2032 N LBU 293	28.614	15.702	18.410	1.00	39.60	B2
ATOM 2033 H LBU 293	30.149	16.513	18.374	1.00	00.00	B2
ATOM 2034 H LBU 293	30.149	16.513	18.374	1.00	00.00	B2
ATOM 2035 CH LBU 293	28.969	17.201	16.138	1.00	34.34	B2
ATOM 2036 CG LBU 293	28.969	17.201	16.138	1.00	34.34	B2
ATOM 2037 CH LBU 293	28.969	17.201	16.138	1.00	34.34	B2
ATOM 2038 CH LBU 293	28.969	17.201	16.138	1.00	34.34	B2
ATOM 2039 CH LBU 293	28.969	17.201	16.138	1.00	34.34	B2
ATOM 2040 CH LBU 293	28.969	17.201	16.138	1.00	34.34	B2
ATOM 2041 CH LBU 293	28.969	17.201	16.138	1.00	34.34	B2
ATOM 2042 CH LBU 293	28.969	17.201	16.138	1.00	34.34	B2
ATOM 2043 CH LBU 293	28.969	17.201	16.138	1.00	34.34	B2
ATOM 2044 CH LBU 293	28.969	17.201	16.138	1.00	34.34	B2
ATOM 2045 CH LBU 293	28.969	17.201	16.138	1.00	34.34	B2
ATOM 2046 CH LBU 293	28.969	17.201	16.138	1.00	34.34	B2
ATOM 2047 CH LBU 293	28.969	17.201	16.138	1.00	34.34	B2
ATOM 2048 CH LBU 293	28.969	17.201	16.138	1.00	34.34	B2
ATOM 2049 CH LBU 293	28.969	17.201	16.138	1.00	34.34	B2
ATOM 2050 CH LBU 293	28.969	17.201	16.138	1.00	34.34	B2
ATOM 2051 CH LBU 293	28.969	17.201	16.138	1.00	34.34	B2
ATOM 2052 CH LBU 293	28.969	17.201	16.138	1.00	34.34	B2
ATOM 2053 CH LBU 293	28.969	17.201	16.138	1.00	34.34	B2
ATOM 2054 CH LBU 293	28.969	17.201	16.138	1.00	34.34	B2
ATOM 2055 CH LBU 293	28.969	17.201	16.138	1.00	34.34	B2
ATOM 2056 CH LBU 293	28.969	17.201	16.138	1.00	34.34	B2
ATOM 2057 CH LBU 293	28.969	17.201	16.138	1.00	34.34	B2
ATOM 2058 CH LBU 293	28.969	17.201	16.138	1.00	34.34	B2
ATOM 2059 CH LBU 293	28.969	17.201	16.138	1.00	34.34	B2
ATOM 2060 CH LBU 293	28.969	17.201	16.138	1.00	34.34	B2
ATOM 2061 CH LBU 293	28.969	17.201	16.138	1.00	34.34	B2
ATOM 2062 CH LBU 293	28.969	17.201	16.138	1.00	34.34	B2
ATOM 2063 CH LBU 293	28.969	17.201	16.138	1.00	34.34	B2
ATOM 2064 CH LBU 293	28.969	17.201	16.138	1.00	34.34	B2
ATOM 2065 CH LBU 293	28.969	17.201	16.138	1.00	34.34	B2
ATOM 2066 CH LBU 293	28.969	17.201	16.138	1.00	34.34	B2
ATOM 2067 CH LBU 293	28.969	17.201	16.138	1.00	34.34	B2
ATOM 2068 CH LBU 293	28.969	17.201	16.138	1.00	34.34	B2
ATOM 2069 CH LBU 293	28.969	17.201	16.138	1.00	34.34	B2
ATOM 2070 CH LBU 293	28.969	17.201	16.138	1.00	34.34	B2
ATOM 2071 CH LBU 293	28.969	17.201	16.138	1.00	34.34	B2
ATOM 2072 CH LBU 293	28.969	17.201	16.138	1.00	34.34	B2
ATOM 2073 CH LBU 293	28.969	17.201	16.138	1.00	34.34	B2
ATOM 2074 CH LBU 293	28.969	17.201	16.138	1.00	34.34	B2
ATOM 2075 CH LBU 293	28.969	17.201	16.138	1.00	34.34	B2
ATOM 2076 CH LBU 293	28.969	17.201	16.138	1.00	34.34	B2
ATOM 2077 CH LBU 293	28.969	17.201	16.138	1.00	34.34	B2
ATOM 2078 CH LBU 293	28.969	17.201	16.138	1.00	34.34	B2
ATOM 2079 CH LBU 293	28.969	17.201	16.138	1.00	34.34	B2
ATOM 2080 CH LBU 293	28.969	17.201	16.138	1.00	34.34	B2
ATOM 2081 CH LBU 293	28.969	17.201	16.138	1.00	34.34	B2
ATOM 2082 CH LBU 293	28.969	17.201	16.138	1.00	34.34	B2
ATOM 2083 CH LBU 293	28.969	17.201	16.138	1.00	34.34	B2
ATOM 2084 CH LBU 293	28.969	17.201	16.138	1.00	34.34	B2
ATOM 2085 CH LBU 293	28.969	17.201	16.138	1.00	34.34	B2
ATOM 2086 CH LBU 293	28.969	17.201	16.138	1.00	34.34	B2
ATOM 2087 CH LBU 293	28.969	17.201	16.138	1.00	34.34	B2
ATOM 2088 CH LBU 293	28.969	17				

FIGURE 5

ATOM 2039 C LEU 293	29.933	14.660	16.596	1.00	40.86	B2
ATOM 2040 O LEU 293	29.686	13.669	15.449	1.00	40.86	B2
ATOM 2041 N GLU 294	32.887	13.495	17.365	1.00	41.12	B2
ATOM 2042 O GLU 294	31.598	12.251	17.000	1.00	41.12	B2
ATOM 2044 CA GLU 294	30.896	10.944	17.485	1.00	42.38	B2
ATOM 2045 CG GLU 294	30.715	10.614	18.972	1.00	56.76	B2
ATOM 2046 CD GLU 294	30.715	10.614	18.972	1.00	56.76	B2
ATOM 2047 OE1 GLU 294	29.958	10.670	20.702	1.00	62.72	B2
ATOM 2048 OE2 GLU 294	29.958	10.670	18.692	1.00	64.81	B2
ATOM 2050 C GLU 294	31.972	12.065	15.632	1.00	41.53	B2
ATOM 2051 N GLV 295	32.424	13.203	15.066	1.00	40.93	B2
ATOM 2052 H GLV 295	32.357	14.033	15.671	1.00	0.00	B2
ATOM 2053 H GLV 295	32.357	14.033	15.671	1.00	0.00	B2
ATOM 2054 C GLV 295	32.073	13.210	12.634	1.00	40.40	B2
ATOM 2055 O GLV 295	32.477	13.216	11.487	1.00	40.56	B2
ATOM 2056 N ILE 296	30.718	13.796	12.038	1.00	41.18	B2
ATOM 2057 CA ILE 296	29.683	14.580	11.009	1.00	43.49	B2
ATOM 2058 CB ILE 296	29.683	14.580	11.009	1.00	43.49	B2
ATOM 2059 CG ILE 296	30.039	17.189	11.063	1.00	46.06	B2
ATOM 2060 CD ILE 296	30.039	17.189	11.063	1.00	46.06	B2
ATOM 2061 CE ILE 296	30.039	17.189	11.063	1.00	46.06	B2
ATOM 2062 C ILE 296	30.718	13.796	12.038	1.00	41.18	B2
ATOM 2063 H ILE 296	30.718	13.796	12.038	1.00	41.18	B2
ATOM 2064 H ILE 296	30.718	13.796	12.038	1.00	41.18	B2
ATOM 2065 N SER 297	30.715	11.875	10.019	1.00	47.21	B2
ATOM 2066 H SER 297	31.526	12.491	9.936	1.00	0.00	B2
ATOM 2067 CA SER 297	30.715	10.644	12.100	1.00	46.73	B2
ATOM 2068 CB SER 297	30.715	10.644	12.100	1.00	46.73	B2
ATOM 2069 CG SER 297	30.948	11.782	7.071	1.00	46.27	B2
ATOM 2070 HC SER 297	30.331	12.000	6.503	1.00	0.00	B2
ATOM 2071 O SER 297	31.120	11.122	9.191	1.00	30.55	B2
ATOM 2072 O SER 297	31.120	11.122	9.191	1.00	30.55	B2
ATOM 2073 N PRO 298	32.655	9.069	8.697	1.00	49.68	B2
ATOM 2074 CA PRO 298	31.782	7.964	8.314	1.00	50.62	B2
ATOM 2075 CB PRO 298	31.782	7.964	8.314	1.00	50.62	B2
ATOM 2076 CD PRO 298	33.948	7.308	7.856	1.00	51.53	B2
ATOM 2077 CG PRO 298	33.576	7.266	7.231	1.00	50.43	B2
ATOM 2078 CH PRO 298	33.576	7.266	7.231	1.00	50.43	B2
ATOM 2079 O PRO 298	32.481	10.137	7.700	1.00	50.50	B2
ATOM 2080 N GLN 299	34.713	10.086	6.469	1.00	50.48	B2
ATOM 2081 H GLN 299	33.779	9.779	6.796	1.00	0.00	B2
ATOM 2082 CA GLN 299	33.898	11.236	4.301	1.00	54.33	B2
ATOM 2083 CG GLN 299	33.095	10.067	3.728	1.00	58.11	B2
ATOM 2084 CD GLN 299	33.095	10.067	3.728	1.00	58.11	B2
ATOM 2085 CE GLN 299	31.140	9.083	4.798	1.00	61.00	B2
ATOM 2087 NE1 GLN 299	30.942	11.217	4.704	1.00	62.17	B2
ATOM 2088 NE2 GLN 299	31.345	11.017	4.400	1.00	0.00	B2
ATOM 2089 NE3 GLN 299	30.924	11.017	4.306	1.00	0.00	B2
ATOM 2090 NE4 GLN 299	30.924	11.017	4.306	1.00	0.00	B2
ATOM 2091 C GLN 299	34.923	12.453	6.160	1.00	51.04	B2
ATOM 2092 N LEU 300	34.792	12.318	7.210	1.00	48.15	B2
ATOM 2093 H LEU 300	34.818	12.918	7.210	1.00	48.15	B2
ATOM 2094 CA LEU 300	33.383	12.518	7.471	1.00	0.00	B2
ATOM 2095 CB LEU 300	33.383	12.518	7.471	1.00	0.00	B2
ATOM 2096 CG LEU 300	32.756	12.428	7.745	1.00	41.12	B2
ATOM 2097 CD LEU 300	32.756	12.428	7.745	1.00	41.12	B2
ATOM 2098 OE1 LEU 300	32.073	15.546	6.974	1.00	27.99	B2
ATOM 2099 OE2 LEU 300	32.073	15.546	6.974	1.00	27.99	B2
ATOM 2100 C LEU 300	31.472	14.874	5.668	1.00	38.24	B2
ATOM 2101 N GLV 301	31.472	14.874	5.668	1.00	38.24	B2
ATOM 2102 H GLV 301	31.472	14.874	5.668	1.00	38.24	B2
ATOM 2103 CA GLV 301	35.157	12.213	9.644	1.00	40.81	B2
ATOM 2104 CB GLV 301	35.157	12.213	9.644	1.00	40.81	B2
ATOM 2105 C GLV 301	35.157	12.213	9.644	1.00	40.81	B2
ATOM 2106 N PRO 302	34.468	11.453	9.985	1.00	37.33	B2
ATOM 2107 CG PRO 302	34.353	12.630	8.790	1.00	37.77	B2
ATOM 2108 CD PRO 302	34.353	12.630	8.790	1.00	37.77	B2
ATOM 2109 CE PRO 302	39.047	11.487	7.745	1.00	37.94	B2
ATOM 2110 CG PRO 302	39.047	11.487	7.745	1.00	37.94	B2
ATOM 2111 C PRO 302	38.486	15.821	10.033	1.00	37.45	B2
ATOM 2112 H THR 303	38.486	15.821	10.033	1.00	37.45	B2
ATOM 2113 N THR 303	38.547	16.311	9.104	1.00	37.05	B2
ATOM 2114 H THR 303	38.085	15.727	8.567	1.00	0.00	B2
ATOM 2115 CA THR 303	38.085	15.727	8.567	1.00	0.00	B2
ATOM 2116 CB THR 303	38.085	15.727	8.567	1.00	0.00	B2
ATOM 2117 CG1 THR 303	37.416	17.181	6.909	1.00	39.64	B2
ATOM 2118 CG2 THR 303	37.416	17.181	6.909	1.00	39.64	B2
ATOM 2119 HCG1 THR 303	37.416	17.181	6.909	1.00	39.64	B2
ATOM 2120 C THR 303	37.416	17.181	6.909	1.00	39.64	B2
ATOM 2121 O THR 303	38.085	19.163	11.063	1.00	33.11	B2
ATOM 2122 H LEU 304	38.436	16.400	10.761	1.00	31.76	B2
ATOM 2123 N LEU 304	38.436	16.400	10.761	1.00	31.76	B2
ATOM 2124 CA LEU 304	38.436	16.400	10.761	1.00	31.76	B2
ATOM 2125 CB LEU 304	38.436	16.400	10.761	1.00	31.76	B2
ATOM 2126 CD LEU 304	38.436	16.400	10.761	1.00	31.76	B2
ATOM 2127 CE LEU 304	38.436	16.400	10.761	1.00	31.76	B2
ATOM 2128 CD2 LEU 304	33.171	17.638	12.309	1.00	38.47	B2
ATOM 2129 H LEU 304	33.171	17.638	12.309	1.00	38.47	B2
ATOM 2130 O LEU 304	37.453	17.726	13.471	1.00	31.86	B2
ATOM 2131 N ASP 305	38.510	16.811	11.326	1.00	30.56	B2
ATOM 2132 H ASP 305	38.510	16.811	11.326	1.00	30.56	B2
ATOM 2133 CA ASP 305	40.504	15.608	14.114	1.00	36.28	B2
ATOM 2134 CB ASP 305	40.504	15.608	14.114	1.00	36.28	B2
ATOM 2135 CG ASP 305	39.912	14.201	14.288	1.00	40.44	B2
ATOM 2136 CD ASP 305	39.912	14.201	14.288	1.00	40.44	B2
ATOM 2137 OE1 ASP 305	40.476	13.906	13.306	1.00	37.52	B2
ATOM 2138 OE2 ASP 305	40.476	13.906	13.306	1.00	37.52	B2
ATOM 2139 O ASP 305	40.476	13.906	13.306	1.00	37.52	B2
ATOM 2140 N THR 306	40.476	13.906	13.306	1.00	37.52	B2

FIGURE 5

ATOM 1141 H THR 306	40.469	12.475	12.230	1.00	0.00	82
ATOM 1142 CA THR 306	41.553	19.633	12.751	1.00	24.39	82
ATOM 1143 CB THR 306	41.665	19.931	11.318	1.00	24.58	82
ATOM 1144 CG THR 306	40.701	19.610	10.713	1.00	24.13	82
ATOM 1145 HG1 THR 306	42.447	18.079	10.764	1.00	0.00	82
ATOM 1146 CG2 THR 306	42.690	21.027	11.089	1.00	15.77	82
ATOM 1147 C THR 306	40.893	20.844	13.419	1.00	25.24	82
ATOM 1148 N THR 306	40.952	20.844	13.419	1.00	25.24	82
ATOM 1149 H THR 306	39.615	21.317	12.586	1.00	14.74	82
ATOM 1150 H LEU 307	39.125	20.547	12.520	1.00	25.91	82
ATOM 1151 CA LEU 307	38.900	22.228	13.764	1.00	25.53	82
ATOM 1152 CB LEU 307	38.950	22.214	15.265	1.00	25.09	82
ATOM 1153 CG LEU 307	38.371	22.197	13.584	1.00	22.93	82
ATOM 1154 CD LEU 307	37.008	22.515	13.484	1.00	28.87	82
ATOM 1155 CE LEU 307	35.311	22.846	12.728	1.00	28.93	82
ATOM 1156 C LEU 307	38.950	22.214	15.265	1.00	25.09	82
ATOM 1157 N LEU 307	38.875	22.214	15.265	1.00	25.09	82
ATOM 1158 H GIN 308	38.871	21.044	15.879	1.00	19.09	82
ATOM 1159 H GIN 308	38.883	20.339	15.319	1.00	0.00	82
ATOM 1160 CA GIN 308	38.374	19.799	17.560	1.00	29.41	82
ATOM 1161 CB GIN 308	37.862	19.140	18.935	1.00	32.24	82
ATOM 1162 CG GIN 308	37.586	17.027	15.165	1.00	34.03	82
ATOM 1163 CD GIN 308	38.053	17.127	10.299	1.00	11.67	82
ATOM 1164 CE GIN 308	38.547	17.697	20.917	1.00	0.00	82
ATOM 1165 HG1 GIN 308	37.735	16.174	20.436	1.00	0.00	82
ATOM 1166 HG2 GIN 308	37.735	16.174	20.436	1.00	0.00	82
ATOM 1167 H GIN 308	40.196	17.786	19.101	1.00	18.44	82
ATOM 1168 N GIN 308	41.269	20.671	17.460	1.00	28.78	82
ATOM 1170 N LEU 309	41.557	20.033	19.957	1.00	24.56	82
ATOM 1171 H LEU 309	43.671	20.154	17.106	1.00	26.54	82
ATOM 1172 CA LEU 309	43.632	18.536	17.241	1.00	24.98	82
ATOM 1173 CG LEU 309	43.952	18.310	16.631	1.00	14.45	82
ATOM 1174 CD LEU 309	42.993	21.416	17.909	1.00	28.24	82
ATOM 1175 CE LEU 309	43.370	21.957	18.907	1.00	30.32	82
ATOM 1176 H LEU 309	42.993	21.416	17.909	1.00	28.24	82
ATOM 1177 C LEU 309	42.993	21.416	17.909	1.00	28.24	82
ATOM 1178 N LEU 309	43.370	21.957	18.907	1.00	30.32	82
ATOM 1179 H LEU 309	42.993	21.416	17.909	1.00	28.24	82
ATOM 1180 N ASP 310	42.798	22.437	16.007	1.00	0.00	82
ATOM 1181 CA ASP 310	42.495	24.477	16.495	1.00	27.90	82
ATOM 1182 CB ASP 310	42.015	24.659	15.076	1.00	26.41	82
ATOM 1183 CG ASP 310	42.959	24.766	15.905	1.00	31.54	82
ATOM 1184 CD ASP 310	42.297	24.314	16.514	1.00	37.72	82
ATOM 1185 CE ASP 310	41.646	24.449	17.216	1.00	37.72	82
ATOM 1186 N VAL 311	40.374	25.086	17.725	1.00	16.29	82
ATOM 1188 N VAL 311	40.374	25.086	17.725	1.00	16.29	82
ATOM 1189 H VAL 311	39.961	24.847	17.225	1.00	0.00	82
ATOM 1190 CA VAL 311	40.374	25.086	17.725	1.00	16.29	82
ATOM 1191 CB VAL 311	39.099	25.217	18.469	1.00	21.47	82
ATOM 2192 CG1 VAL 311	37.241	25.455	19.949	1.00	19.04	82
ATOM 2193 CG2 VAL 311	37.261	25.488	17.667	1.00	16.56	82
ATOM 2194 C VAL 311	40.270	25.638	20.020	1.00	27.21	82
ATOM 2195 N VAL 311	40.267	25.647	20.019	1.00	27.21	82
ATOM 2196 H VAL 311	40.385	25.654	19.536	1.00	0.00	82
ATOM 2197 H ALA 312	40.585	25.674	19.536	1.00	0.00	82
ATOM 2198 CA ALA 312	41.515	24.137	21.583	1.00	21.21	82
ATOM 2199 CB ALA 312	41.515	24.137	21.583	1.00	21.21	82
ATOM 2200 CG ALA 312	41.515	24.137	21.583	1.00	21.21	82
ATOM 2201 CD ALA 312	41.515	24.137	21.583	1.00	21.21	82
ATOM 2202 N ASP 313	43.554	25.286	20.735	1.00	31.33	82
ATOM 2203 H ASP 313	43.431	24.730	19.935	1.00	41.09	82
ATOM 2204 CA ASP 313	43.431	24.730	19.935	1.00	41.09	82
ATOM 2205 CB ASP 313	45.279	26.512	19.447	1.00	38.87	82
ATOM 2206 CG ASP 313	46.071	25.404	18.866	1.00	44.55	82
ATOM 2207 CD ASP 313	46.255	25.439	17.636	1.00	48.67	82
ATOM 2208 C ASP 313	44.187	27.599	17.659	1.00	35.12	82
ATOM 2209 N ASP 313	44.187	27.599	17.659	1.00	35.12	82
ATOM 2210 O ASP 313	44.807	28.390	21.894	1.00	38.60	82
ATOM 2211 H PHE 314	42.784	27.665	19.819	1.00	0.00	82
ATOM 2212 H PHE 314	42.784	27.665	19.819	1.00	0.00	82
ATOM 2213 CA PHE 314	41.572	29.660	20.600	1.00	31.09	82
ATOM 2214 CB PHE 314	41.572	29.660	20.600	1.00	31.09	82
ATOM 2215 CG PHE 314	41.572	29.660	20.600	1.00	31.09	82
ATOM 2216 CD PHE 314	39.780	31.568	19.247	1.00	31.81	82
ATOM 2217 CE PHE 314	41.907	32.354	20.021	1.00	35.65	82
ATOM 2218 C PHE 314	39.318	32.857	19.240	1.00	29.15	82
ATOM 2219 H PHE 314	40.154	33.870	19.622	1.00	31.81	82
ATOM 2220 C PHE 314	40.154	33.870	19.622	1.00	31.81	82
ATOM 2221 C PHE 314	42.282	29.601	22.057	1.00	29.90	82
ATOM 2222 H PHE 314	41.588	28.332	22.384	1.00	29.29	82
ATOM 2223 O PHE 314	41.588	28.332	22.384	1.00	29.29	82
ATOM 2224 H ALA 315	41.448	27.764	22.021	1.00	0.00	82
ATOM 2225 CA ALA 315	41.300	28.583	23.961	1.00	31.61	82
ATOM 2226 CB ALA 315	41.300	28.583	23.961	1.00	31.61	82
ATOM 2227 C ALA 315	42.282	29.601	22.057	1.00	29.90	82
ATOM 2228 O ALA 315	42.282	29.601	22.057	1.00	29.90	82
ATOM 2229 H THR 316	42.361	29.437	25.853	1.00	37.66	82
ATOM 2230 H THR 316	42.361	29.437	25.853	1.00	37.66	82
ATOM 2231 CA THR 316	44.760	28.388	23.374	1.00	37.09	82
ATOM 2232 CB THR 316	45.795	27.355	25.136	1.00	41.16	82
ATOM 2233 CG1 THR 316	45.795	27.355	25.136	1.00	41.16	82
ATOM 2234 CG2 THR 316	45.795	27.355	25.136	1.00	41.16	82
ATOM 2235 C THR 316	47.132	27.415	25.888	1.00	40.31	82
ATOM 2236 C THR 316	45.458	29.710	25.177	1.00	36.47	82
ATOM 2237 H THR 316	45.458	29.710	25.177	1.00	36.47	82
ATOM 2238 H THR 316	45.458	29.710	25.177	1.00	36.47	82
ATOM 2239 H THR 317	45.610	30.287	23.970	1.00	46.53	82
ATOM 2240 CA THR 317	46.092	31.657	23.844	1.00	37.03	82
ATOM 2241 CB THR 317	46.092	31.657	23.844	1.00	37.03	82
ATOM 2242 CG1 THR 317	46.092	31.657	23.844	1.00	37.03	82
ATOM 2243 CG2 THR 317	46.092	31.657	23.844	1.00	37.03	82
ATOM 2244 C THR 317	46.752	31.352	21.575	1.00	35.11	82

FIGURES

ATOM 2243 H21 THR 317	46.489	35.043	21.389	1.00	0.00	B2
ATOM 2244 CG1 THR 317	46.189	35.566	21.383	1.00	0.00	B2
ATOM 2245 C THR 317	45.338	35.597	24.832	1.00	19.30	B2
ATOM 2246 O THR 317	45.994	33.378	35.583	1.00	-0.17	B2
ATOM 2247 H1 THR 317	45.994	33.378	35.583	1.00	-0.17	B2
ATOM 2248 H2 THR 317	45.994	33.378	35.583	1.00	-0.17	B2
ATOM 2249 CA HE 318	43.177	33.317	35.788	1.00	-0.75	B2
ATOM 2250 CB HE 318	41.821	31.979	35.667	1.00	37.17	B2
ATOM 2251 CD HE 318	41.821	31.979	35.667	1.00	37.17	B2
ATOM 2252 CG HE 318	41.216	33.313	24.160	1.00	31.49	B2
ATOM 2253 CD HE 318	41.626	34.657	23.614	1.00	19.66	B2
ATOM 2254 C HE 318	41.624	33.019	27.717	1.00	42.43	B2
ATOM 2255 N HE 318	43.537	31.008	27.163	1.00	0.00	B2
ATOM 2256 H THR 319	43.663	31.784	27.744	1.00	44.17	B2
ATOM 2257 H THR 319	43.537	31.008	27.163	1.00	0.00	B2
ATOM 2258 CA THR 319	43.893	31.633	29.547	1.00	46.90	B2
ATOM 2259 CB THR 319	43.893	31.633	29.547	1.00	46.90	B2
ATOM 2260 CG THR 319	43.994	30.094	31.131	1.00	56.05	B2
ATOM 2261 CD THR 319	43.005	30.997	32.038	1.00	56.61	B2
ATOM 2262 CE THR 319	45.184	29.788	31.760	1.00	58.07	B2
ATOM 2263 CD THR 319	45.184	29.788	31.760	1.00	58.07	B2
ATOM 2264 CD THR 319	45.184	29.788	31.760	1.00	58.07	B2
ATOM 2265 HE1 THR 319	45.824	29.788	31.760	1.00	60.07	B2
ATOM 2266 HE2 THR 319	45.824	29.788	31.760	1.00	60.07	B2
ATOM 2267 CE2 THR 319	43.044	30.512	34.456	1.00	61.00	B2
ATOM 2268 CE3 THR 319	43.032	30.967	33.210	1.00	61.58	B2
ATOM 2269 CE4 THR 319	43.032	30.967	33.210	1.00	61.58	B2
ATOM 2270 C THR 319	45.398	32.136	29.456	1.00	47.85	B2
ATOM 2271 N THR 319	45.635	31.772	30.990	1.00	47.99	B2
ATOM 2272 H1 THR 319	46.338	31.915	28.550	1.00	48.63	B2
ATOM 2273 H2 THR 319	46.338	31.915	28.550	1.00	48.63	B2
ATOM 2274 CA GLN 320	47.706	32.319	28.767	1.00	49.45	B2
ATOM 2275 CB GLN 320	48.567	31.988	27.859	1.00	51.44	B2
ATOM 2276 CD GLN 320	48.567	31.988	27.859	1.00	51.44	B2
ATOM 2277 CE GLN 320	49.851	30.469	26.434	1.00	60.17	B2
ATOM 2278 OE1 GLN 320	51.116	30.465	26.434	1.00	65.26	B2
ATOM 2279 HE1 GLN 320	49.771	30.465	25.133	1.00	59.32	B2
ATOM 2280 HE2 GLN 320	49.771	30.465	25.133	1.00	59.32	B2
ATOM 2281 C GLN 320	50.582	30.081	24.590	1.00	60.00	B2
ATOM 2282 CG GLN 320	47.717	32.790	26.983	1.00	49.62	B2
ATOM 2283 O GLN 320	48.251	32.709	29.987	1.00	49.91	B2
ATOM 2284 H1 GLN 321	46.335	34.027	27.463	1.00	0.00	B2
ATOM 2285 H2 GLN 321	46.335	34.027	27.463	1.00	0.00	B2
ATOM 2286 CA GLN 321	46.837	35.988	28.271	1.00	52.08	B2
ATOM 2287 CB GLN 321	46.837	35.988	28.271	1.00	52.08	B2
ATOM 2288 CD GLN 321	47.211	38.781	27.100	1.00	53.13	B2
ATOM 2289 CE GLN 321	47.211	38.781	27.100	1.00	53.13	B2
ATOM 2290 OE1 GLN 321	48.090	38.622	26.864	1.00	55.36	B2
ATOM 2291 OE2 GLN 321	48.090	38.622	26.864	1.00	55.36	B2
ATOM 2292 HE1 GLN 321	46.830	39.713	28.889	1.00	0.00	B2
ATOM 2293 HE2 GLN 321	46.830	39.713	28.889	1.00	0.00	B2
ATOM 2294 CG PHE 341	48.338	-0.057	28.168	1.00	0.00	B2
ATOM 2295 CD PHE 341	48.338	-0.057	28.168	1.00	0.00	B2
ATOM 2296 CE PHE 341	48.338	-0.057	28.168	1.00	0.00	B2
ATOM 2297 H1 MET 332	46.112	36.315	28.562	1.00	53.40	B2
ATOM 2298 H2 MET 332	46.112	36.315	28.562	1.00	53.40	B2
ATOM 2299 C MET 332	45.709	34.421	30.058	1.00	54.39	B2
ATOM 2300 O MET 332	45.098	34.592	29.662	1.00	45.40	B2
ATOM 2301 H MET 332	44.619	35.748	31.375	1.00	45.42	B2
ATOM 2302 H MET 332	44.619	35.748	31.375	1.00	45.42	B2
ATOM 2303 CA MET 332	42.327	34.865	30.189	1.00	51.76	B2
ATOM 2304 CB MET 332	42.327	34.865	30.189	1.00	51.76	B2
ATOM 2305 SD MET 332	40.861	34.428	31.199	1.00	54.19	B2
ATOM 2306 SE MET 332	40.793	33.197	30.069	1.00	52.53	B2
ATOM 2307 H MET 332	40.793	33.197	30.069	1.00	52.53	B2
ATOM 2308 O MET 332	45.781	36.719	33.748	1.00	57.85	B2
ATOM 2309 N GLU 333	46.652	34.900	32.319	1.00	60.78	B2
ATOM 2310 CA GLU 333	46.652	34.900	32.319	1.00	60.78	B2
ATOM 2311 CB GLU 333	47.941	34.796	31.544	1.00	63.00	B2
ATOM 2312 CD GLU 333	48.538	33.613	31.937	1.00	65.81	B2
ATOM 2313 CE GLU 333	47.640	32.423	32.918	1.00	64.36	B2
ATOM 2314 CF GLU 333	48.565	33.161	33.000	1.00	71.19	B2
ATOM 2315 CG1 GLU 333	49.451	30.900	32.884	1.00	72.43	B2
ATOM 2316 CG2 GLU 333	48.648	36.124	33.418	1.00	63.96	B2
ATOM 2317 H1 GLU 333	47.559	17.690	25.056	1.00	62.56	B2
ATOM 2318 H2 GLU 333	47.559	17.690	25.056	1.00	62.56	B2
ATOM 2319 CE MET 338	27.338	21.232	25.515	1.00	65.50	B2
ATOM 2320 CD MET 338	27.338	21.232	25.515	1.00	65.50	B2
ATOM 2321 O MET 338	25.375	17.061	27.500	1.00	0.00	B2
ATOM 2322 H1 MET 338	26.325	16.010	26.594	1.00	0.00	B2
ATOM 2323 H2 MET 338	26.325	16.010	26.594	1.00	0.00	B2
ATOM 2324 CA MET 338	27.108	17.107	27.620	1.00	0.00	B2
ATOM 2325 CB MET 338	27.108	17.107	27.620	1.00	0.00	B2
ATOM 2326 CD MET 338	26.726	17.853	25.851	1.00	60.35	B2
ATOM 2327 CE MET 338	24.493	17.810	23.998	1.00	55.58	B2
ATOM 2328 CF MET 338	25.375	17.061	27.500	1.00	57.55	B2
ATOM 2329 CA PHE 339	23.463	18.098	21.903	1.00	53.52	B2
ATOM 2330 CB PHE 339	23.463	18.098	21.903	1.00	53.52	B2
ATOM 2331 CD PHE 339	23.463	18.098	21.903	1.00	53.52	B2
ATOM 2332 CE PHE 339	23.463	18.098	21.903	1.00	53.52	B2
ATOM 2333 O PHE 339	24.700	15.025	22.333	1.00	54.37	B2
ATOM 2334 N ALA 340	22.704	15.025	22.333	1.00	54.37	B2
ATOM 2335 CA ALA 340	22.704	15.025	22.333	1.00	54.37	B2
ATOM 2336 CB ALA 340	22.704	15.025	22.333	1.00	54.37	B2
ATOM 2337 CD ALA 340	22.704	15.025	22.333	1.00	54.37	B2
ATOM 2338 CE ALA 340	22.704	15.025	22.333	1.00	54.37	B2
ATOM 2339 O PHE 341	23.432	13.783	20.195	1.00	55.61	B2
ATOM 2340 N PHE 341	23.432	13.783	20.195	1.00	55.61	B2
ATOM 2341 H1 PHE 341	24.472	13.607	19.685	1.00	0.00	B2
ATOM 2342 H2 PHE 341	24.472	13.607	19.685	1.00	0.00	B2
ATOM 2343 CB PHE 341	24.050	14.541	17.658	1.00	48.16	B2
ATOM 2344 CG PHE 341	24.382	15.940	17.658	1.00	45.00	B2

FIGURE 5

ATOM 2345	CDI	H	341	23.510	16.913	17.359	1.00	-41.44	83
ATOM 2346	CDI	H	341	25.327	16.175	18.388	1.00	-47.03	83
ATOM 2347	CDI	H	341	25.327	17.422	17.483	1.00	-45.15	83
ATOM 2348	CDI	H	341	24.952	18.437	18.580	1.00	-48.36	83
ATOM 2349	CDI	H	341	21.684	12.510	17.672	1.00	-45.36	83
ATOM 2350	CDI	H	341	21.684	13.757	17.672	1.00	-45.36	83
ATOM 2351	O	HIE	341	21.684	12.510	17.672	1.00	-45.36	83
ATOM 2352	N	ALA	342	21.685	11.985	18.745	1.00	-47.46	83
ATOM 2353	N	ALA	342	21.036	12.385	18.741	1.00	-47.46	83
ATOM 2354	N	ALA	342	18.167	10.650	17.997	1.00	-46.11	83
ATOM 2355	C	ALA	342	20.962	10.149	16.536	1.00	-44.37	83
ATOM 2356	C	ALA	342	20.138	9.347	16.418	1.00	-45.65	83
ATOM 2357	O	ALA	342	22.191	11.471	13.382	1.00	-38.10	83
ATOM 2358	H	ALA	342	22.191	11.471	13.382	1.00	-38.10	83
ATOM 2359	H	ALA	342	22.191	11.471	13.382	1.00	-38.10	83
ATOM 2360	CA	SEB	343	21.274	9.523	14.145	1.00	-38.80	83
ATOM 2361	CA	SEB	343	18.842	10.138	13.656	1.00	-38.79	83
ATOM 2362	CA	SEB	343	21.274	9.523	14.145	1.00	-38.80	83
ATOM 2363	HG	SEB	343	18.963	11.055	13.692	1.00	-40.00	83
ATOM 2364	C	SEB	343	22.172	10.667	13.048	1.00	-38.22	83
ATOM 2365	H	SEB	343	22.172	10.667	13.048	1.00	-38.22	83
ATOM 2366	N	ALA	344	21.762	8.978	11.805	1.00	-40.00	83
ATOM 2367	N	ALA	344	21.762	8.978	11.805	1.00	-40.00	83
ATOM 2368	CA	ALA	344	22.914	10.384	10.715	1.00	-18.09	83
ATOM 2369	CA	ALA	344	22.914	10.384	10.715	1.00	-18.09	83
ATOM 2370	C	ALA	344	22.427	11.642	10.946	1.00	-37.71	83
ATOM 2371	O	ALA	344	23.171	12.665	10.676	1.00	-38.42	83
ATOM 2372	N	HIE	345	25.194	12.662	10.163	1.00	-36.10	83
ATOM 2373	N	HIE	345	25.194	12.662	10.163	1.00	-36.10	83
ATOM 2374	CA	HIE	345	20.564	13.358	10.195	1.00	-14.69	83
ATOM 2375	CA	HIE	345	19.040	13.358	10.178	1.00	-32.24	83
ATOM 2376	CDI	HIE	345	17.765	15.343	8.745	1.00	-26.99	83
ATOM 2377	CDI	HIE	345	17.765	15.343	8.745	1.00	-26.99	83
ATOM 2378	CDI	HIE	345	17.765	15.343	8.745	1.00	-26.99	83
ATOM 2379	CDI	HIE	345	17.765	15.343	8.745	1.00	-26.99	83
ATOM 2380	CDI	HIE	345	17.765	15.343	8.745	1.00	-26.99	83
ATOM 2381	CE	HIE	345	17.581	17.201	9.520	1.00	-31.44	83
ATOM 2382	C	HIE	345	20.888	14.455	11.458	1.00	-35.02	83
ATOM 2383	C	HIE	345	20.888	14.455	11.458	1.00	-35.02	83
ATOM 2384	N	ALA	346	20.516	13.468	12.691	1.00	-32.53	83
ATOM 2385	N	ALA	346	20.516	13.468	12.691	1.00	-32.53	83
ATOM 2386	CA	ALA	346	21.156	14.348	12.758	1.00	-31.46	83
ATOM 2387	CA	ALA	346	21.156	14.348	12.758	1.00	-31.46	83
ATOM 2388	CG	ALA	346	19.459	14.284	15.174	1.00	-35.68	83
ATOM 2389	CG	ALA	346	18.788	13.658	16.344	1.00	-38.48	83
ATOM 2390	CG	ALA	346	18.788	13.658	16.344	1.00	-38.48	83
ATOM 2391	CG	ALA	346	18.788	13.658	16.344	1.00	-38.48	83
ATOM 2392	HE21	ALA	346	17.508	13.463	16.167	1.00	-41.08	83
ATOM 2393	HE21	ALA	346	17.508	13.463	16.167	1.00	-41.08	83
ATOM 2394	HE21	ALA	346	17.508	13.463	16.167	1.00	-41.08	83
ATOM 2395	O	ALA	346	22.766	16.251	14.051	1.00	-18.18	83
ATOM 2396	H	ALA	347	23.507	14.910	13.431	1.00	-35.57	83
ATOM 2397	H	ALA	347	23.507	14.910	13.431	1.00	-35.57	83
ATOM 2398	CA	ALA	347	24.907	14.518	13.196	1.00	-36.29	83
ATOM 2399	CA	ALA	347	24.907	14.518	13.196	1.00	-36.29	83
ATOM 2400	CDI	ALA	347	26.986	13.246	14.549	1.00	-37.41	83
ATOM 2401	CDI	ALA	347	26.986	13.246	14.549	1.00	-37.41	83
ATOM 2402	NE	ALA	347	26.072	10.167	14.618	1.00	-47.18	83
ATOM 2403	NE	ALA	347	26.072	10.167	14.618	1.00	-47.18	83
ATOM 2404	CDI	ALA	347	26.072	10.167	14.618	1.00	-47.18	83
ATOM 2405	NE	ALA	347	26.918	9.802	11.882	1.00	-50.41	83
ATOM 2406	NE	ALA	347	26.918	9.802	11.882	1.00	-50.41	83
ATOM 2407	NE	ALA	347	26.918	9.802	11.882	1.00	-50.41	83
ATOM 2408	NE	ALA	347	26.918	9.802	11.882	1.00	-50.41	83
ATOM 2409	NE	ALA	347	26.918	9.802	11.882	1.00	-50.41	83
ATOM 2410	NE	ALA	347	26.918	9.802	11.882	1.00	-50.41	83
ATOM 2411	O	ALA	347	25.135	8.133	11.697	1.00	-40.00	83
ATOM 2412	O	ALA	347	25.135	8.133	11.697	1.00	-40.00	83
ATOM 2413	N	ALA	348	24.811	15.353	11.096	1.00	-34.74	83
ATOM 2414	N	ALA	348	24.811	15.353	11.096	1.00	-34.74	83
ATOM 2415	CA	ALA	348	24.802	16.235	9.954	1.00	-35.76	83
ATOM 2416	CA	ALA	348	24.802	16.235	9.954	1.00	-35.76	83
ATOM 2417	CA	ALA	348	24.802	16.235	9.954	1.00	-35.76	83
ATOM 2418	CA	ALA	348	24.802	16.235	9.954	1.00	-35.76	83
ATOM 2419	NE	ALA	348	24.705	12.990	2.457	1.00	-54.72	83
ATOM 2420	NE	ALA	348	24.705	12.990	2.457	1.00	-54.72	83
ATOM 2421	NE	ALA	348	24.705	12.990	2.457	1.00	-54.72	83
ATOM 2422	NE	ALA	348	24.705	12.990	2.457	1.00	-54.72	83
ATOM 2423	NE	ALA	348	24.705	12.990	2.457	1.00	-54.72	83
ATOM 2424	NE	ALA	348	24.705	12.990	2.457	1.00	-54.72	83
ATOM 2425	NE	ALA	348	24.705	12.990	2.457	1.00	-54.72	83
ATOM 2426	NE	ALA	348	24.705	12.990	2.457	1.00	-54.72	83
ATOM 2427	NE	ALA	348	24.705	12.990	2.457	1.00	-54.72	83
ATOM 2428	NE	ALA	348	24.705	12.990	2.457	1.00	-54.72	83
ATOM 2429	O	ALA	348	23.524	12.329	5.319	1.00	-40.00	83
ATOM 2430	O	ALA	348	23.524	12.329	5.319	1.00	-40.00	83
ATOM 2431	O	ALA	348	23.524	12.329	5.319	1.00	-40.00	83
ATOM 2432	O	ALA	348	23.524	12.329	5.319	1.00	-40.00	83
ATOM 2433	CA	ALA	349	23.352	10.083	6.445	1.00	-40.00	83
ATOM 2434	CA	ALA	349	23.352	10.083	6.445	1.00	-40.00	83
ATOM 2435	CA	ALA	349	23.352	10.083	6.445	1.00	-40.00	83
ATOM 2436	CA	ALA	349	23.352	10.083	6.445	1.00	-40.00	83
ATOM 2437	CA	ALA	349	23.352	10.083	6.445	1.00	-40.00	83
ATOM 2438	CA	ALA	349	23.352	10.083	6.445	1.00	-40.00	83
ATOM 2439	CA	ALA	349	23.352	10.083	6.445	1.00	-40.00	83
ATOM 2440	CA	ALA	349	23.352	10.083	6.445	1.00	-40.00	83
ATOM 2441	CA	ALA	349	23.352	10.083	6.445	1.00	-40.00	83
ATOM 2442	CA	ALA	349	23.352	10.083	6.445	1.00	-40.00	83
ATOM 2443	CA	ALA	349	23.352	10.083	6.445	1.00	-40.00	83
ATOM 2444	CA	ALA	349	23.352	10.083	6.445	1.00	-40.00	83
ATOM 2445	CA	ALA	349	23.352	10.083	6.445	1.00	-40.00	83
ATOM 2446	CA	ALA	349	23.352	10.083	6.445	1.00	-40.00	83
ATOM 2447	CA	ALA	349	23.352	10.083	6.445	1.00	-40.00	83
ATOM 2448	CA	ALA	349	23.352	10.083	6.445	1.00	-40.00	83
ATOM 2449	CA	ALA	349	23.352	10.083	6.445	1.00	-40.00	83
ATOM 2450	CA	ALA	349	23.352	10.083	6.445	1.00	-40.00	83
ATOM 2451	CA	ALA	349	23.352	10.083	6.445	1.00	-40.00	83
ATOM 2452	CA	ALA	349	23.352	10.083	6.445	1.00	-40.00	83
ATOM 2453	CA	ALA	349	23.352	10.083	6.445	1.00	-40.00	83
ATOM 2454	CA	ALA	349	23.352	10.083	6.445	1.00	-40.00	83
ATOM 2455	CA	ALA	349	23.352	10.083	6.445	1.00	-40.00	83
ATOM 2456	CA	ALA	349	23.352	10.083	6.445	1.00	-40.00	83
ATOM 2457	CA	ALA	349	23.352	10.083	6.445	1.00	-40.00	83
ATOM 2458	CA	ALA	349	23.352	10.083	6.445	1.00	-40.00	83
ATOM 2459	CA	ALA	349	23.352	10.083	6.445	1.00	-40.00	83
ATOM 2460	CA	ALA	349	23.352	10.083	6.445	1.00	-40.00	83
ATOM 2461	CA	ALA	349	23.352	10.083	6.445	1.00	-40.00	83
ATOM 2462	CA	ALA	349	23.352	10.083	6.445	1.00	-40.00	83
ATOM 2463	CA	ALA	349	23.352	10.083	6.445	1.00	-40.00	83
ATOM 2464	CA	ALA	349	23.352	10.083	6.445	1.00	-40.00	83
ATOM 2465	CA	ALA	349	23.352	10.083	6.445	1.00	-40.00	83
ATOM 2466	CA	ALA	349	23.352	10.083	6.445	1.00	-40.00	83
ATOM 2467	CA	ALA	349	23.352	10.083	6.445	1.00	-40.00	83
ATOM 2468	CA	ALA	349	23.352	10.083	6.445	1.00	-40.00	83
ATOM 2469	CA	ALA	349	23.352	10.083	6.445	1.00	-40.00	83
ATOM 2470	CA	ALA	349	23.352	10.083	6.445	1.00	-40.00	83
ATOM 2471	CA	ALA	349	23.352	10.083	6.445	1.00	-40.00	83
ATOM 2472	CA	ALA	349	23.352	10.083	6.445	1.00	-40.00	83
ATOM 2473	CA	ALA	349	23.352	10.083	6.445	1.00	-40.00	83
ATOM 2474	CA	ALA	349	23.352	10.083	6.445	1.00	-40.00	83
ATOM 2475	CA								

FIGURE 5

ATOM	2447	II	VAL	352	75.0579	20.484	10.314	10.01	0.00	B1	ATOM	2498	N	LEU	358	29.830	28.637	15.383	1.00	28.35	B1
ATOM	2448	II	VAL	352	26.870	20.484	10.314	10.01	0.00	B1	ATOM	2499	N	LEU	358	29.832	27.761	14.997	1.00	28.35	B1
ATOM	2449	CH	VAL	352	24.627	21.432	9.004	1.00	28.96	B1	ATOM	2500	CA	LEU	358	29.832	27.761	14.997	1.00	28.35	B1
ATOM	2450	CH	VAL	352	24.627	21.432	9.004	1.00	28.96	B1	ATOM	2501	CA	LEU	358	29.832	27.761	14.997	1.00	28.35	B1
ATOM	2451	CG2	VAL	352	24.627	21.432	9.004	1.00	28.96	B1	ATOM	2502	CG	LEU	358	33.457	27.761	15.384	1.00	20.42	B1
ATOM	2452	O	VAL	352	26.830	21.709	10.890	1.00	29.79	B1	ATOM	2503	CG	LEU	358	33.457	27.761	15.384	1.00	20.42	B1
ATOM	2453	O	VAL	352	26.830	21.709	10.890	1.00	29.79	B1	ATOM	2504	CG	LEU	358	33.457	27.761	15.384	1.00	20.42	B1
ATOM	2454	CH	VAL	352	24.923	23.543	11.817	1.00	27.32	B1	ATOM	2505	CH	LEU	358	31.727	30.939	15.778	1.00	27.12	B1
ATOM	2455	CH	VAL	352	24.923	23.543	11.817	1.00	27.32	B1	ATOM	2506	CH	LEU	358	31.727	30.939	15.778	1.00	27.12	B1
ATOM	2456	CA	VAL	353	24.635	24.544	12.819	1.00	26.78	B1	ATOM	2507	CA	LEU	359	31.727	30.939	15.778	1.00	27.12	B1
ATOM	2457	CA	LEU	353	23.484	24.141	13.636	1.00	27.87	B1	ATOM	2508	CA	LEU	359	31.727	30.939	15.778	1.00	27.12	B1
ATOM	2458	CG	LEU	353	22.094	24.034	13.311	1.00	26.54	B1	ATOM	2509	CA	LEU	359	31.727	30.939	15.778	1.00	27.12	B1
ATOM	2459	CG2	LEU	353	22.094	24.034	13.311	1.00	26.54	B1	ATOM	2510	CG	LEU	359	31.727	30.939	15.778	1.00	27.12	B1
ATOM	2460	CG2	LEU	353	21.150	23.732	12.700	1.00	28.27	B1	ATOM	2511	CG	LEU	359	31.727	30.939	15.778	1.00	27.12	B1
ATOM	2461	CG2	LEU	353	21.150	23.732	12.700	1.00	28.27	B1	ATOM	2512	CG	LEU	359	31.727	30.939	15.778	1.00	27.12	B1
ATOM	2462	CH	LEU	353	25.742	24.905	13.772	1.00	27.17	B1	ATOM	2513	CH	LEU	359	31.727	30.939	15.778	1.00	27.12	B1
ATOM	2463	CH	LEU	353	25.742	24.905	13.772	1.00	27.17	B1	ATOM	2514	CH	LEU	359	31.727	30.939	15.778	1.00	27.12	B1
ATOM	2464	CH	VAL	354	26.313	22.096	14.008	1.00	28.00	B1	ATOM	2515	CH	LEU	359	31.727	30.939	15.778	1.00	27.12	B1
ATOM	2465	CA	VAL	354	26.313	22.096	14.008	1.00	28.00	B1	ATOM	2516	CH	LEU	359	31.727	30.939	15.778	1.00	27.12	B1
ATOM	2466	CA	VAL	354	26.313	22.096	14.008	1.00	28.00	B1	ATOM	2517	CH	LEU	359	31.727	30.939	15.778	1.00	27.12	B1
ATOM	2467	CG	VAL	354	28.736	22.910	15.745	1.00	24.62	B1	ATOM	2518	CG	VAL	360	28.736	22.910	15.745	1.00	24.62	B1
ATOM	2468	CG2	VAL	354	28.736	22.910	15.745	1.00	24.62	B1	ATOM	2519	CG	VAL	360	28.736	22.910	15.745	1.00	24.62	B1
ATOM	2469	CG2	VAL	354	27.716	22.167	16.402	1.00	25.36	B1	ATOM	2520	CG	VAL	360	27.716	22.167	16.402	1.00	25.36	B1
ATOM	2470	CH	VAL	354	28.812	24.493	14.337	1.00	25.46	B1	ATOM	2521	CH	VAL	360	27.716	22.167	16.402	1.00	25.36	B1
ATOM	2471	CH	VAL	354	28.812	24.493	14.337	1.00	25.46	B1	ATOM	2522	CH	VAL	360	27.716	22.167	16.402	1.00	25.36	B1
ATOM	2472	II	ALA	355	30.025	25.180	12.235	1.00	26.54	B1	ATOM	2523	CH	VAL	360	27.716	22.167	16.402	1.00	25.36	B1
ATOM	2473	CA	ALA	355	30.025	25.180	12.235	1.00	26.54	B1	ATOM	2524	CH	VAL	360	27.716	22.167	16.402	1.00	25.36	B1
ATOM	2474	CA	ALA	355	30.025	25.180	12.235	1.00	26.54	B1	ATOM	2525	CH	VAL	360	27.716	22.167	16.402	1.00	25.36	B1
ATOM	2475	CG	ALA	355	35.679	28.908	10.900	1.00	29.75	B1	ATOM	2526	CH	VAL	360	27.716	22.167	16.402	1.00	25.36	B1
ATOM	2476	O	ALA	355	30.315	27.484	12.344	1.00	31.93	B1	ATOM	2527	CH	VAL	360	27.716	22.167	16.402	1.00	25.36	B1
ATOM	2477	N	SER	356	32.271	26.484	11.021	1.00	30.30	B1	ATOM	2528	CH	VAL	360	27.716	22.167	16.402	1.00	25.36	B1
ATOM	2478	N	SER	356	32.271	26.484	11.021	1.00	30.30	B1	ATOM	2529	CH	VAL	360	27.716	22.167	16.402	1.00	25.36	B1
ATOM	2479	CA	SER	356	26.901	28.147	11.016	1.00	33.13	B1	ATOM	2530	CH	VAL	360	27.716	22.167	16.402	1.00	25.36	B1
ATOM	2480	CA	SER	356	26.901	28.147	11.016	1.00	33.13	B1	ATOM	2531	CH	VAL	360	27.716	22.167	16.402	1.00	25.36	B1
ATOM	2481	CG	SER	356	35.679	28.908	10.900	1.00	43.87	B1	ATOM	2532	CH	VAL	360	27.716	22.167	16.402	1.00	25.36	B1
ATOM	2482	CG	SER	356	35.679	28.908	10.900	1.00	43.87	B1	ATOM	2533	CH	VAL	360	27.716	22.167	16.402	1.00	25.36	B1
ATOM	2483	CH	SER	356	35.679	28.908	10.900	1.00	29.75	B1	ATOM	2534	CH	VAL	360	27.716	22.167	16.402	1.00	25.36	B1
ATOM	2484	O	SER	356	27.743	29.098	1.900	1.00	29.75	B1	ATOM	2535	CH	VAL	360	27.716	22.167	16.402	1.00	25.36	B1
ATOM	2485	O	SER	356	27.743	29.098	1.900	1.00	29.75	B1	ATOM	2536	CH	VAL	360	27.716	22.167	16.402	1.00	25.36	B1
ATOM	2486	CH	SER	357	27.465	28.464	10.215	1.00	27.82	B1	ATOM	2537	CH	VAL	361	31.028	33.921	21.602	1.00	21.46	B1
ATOM	2487	CH	SER	357	27.465	28.464	10.215	1.00	27.82	B1	ATOM	2538	CH	VAL	361	31.028	33.921	21.602	1.00	21.46	B1
ATOM	2488	CA	SER	357	27.434	28.159	15.559	1.00	26.58	B1	ATOM	2539	CA	SER	361	32.914	34.979	16.441	1.00	26.76	B1
ATOM	2489	CA	SER	357	27.434	28.159	15.559	1.00	26.58	B1	ATOM	2540	CA	SER	361	32.914	34.979	16.441	1.00	26.76	B1
ATOM	2490	CG	SER	357	28.735	28.365	16.105	1.00	33.77	B1	ATOM	2541	CG	SER	361	32.914	34.979	16.441	1.00	26.76	B1
ATOM	2491	CG	SER	357	28.735	28.365	16.105	1.00	33.77	B1	ATOM	2542	CG	SER	361	32.914	34.979	16.441	1.00	26.76	B1
ATOM	2492	CH	SER	357	24.277	27.963	16.913	1.00	28.43	B1	ATOM	2543	CH	SER	362	35.452	31.925	15.318	1.00	18.18	B1
ATOM	2493	CH	SER	357	24.277	27.963	16.913	1.00	28.43	B1	ATOM	2544	CH	SER	362	35.452	31.925	15.318	1.00	18.18	B1
ATOM	2494	CH	SER	357	24.456	27.632	17.120	1.00	26.80	B1	ATOM	2545	CH	SER	362	35.452	31.925	15.318	1.00	18.18	B1
ATOM	2495	CH	SER	357	22.576	28.480	14.495	1.00	29.48	B1	ATOM	2546	CH	SER	362	35.452	31.925	15.318	1.00	18.18	B1
ATOM	2496	CH	SER	357	22.576	28.480	14.495	1.00	29.48	B1	ATOM	2547	CH	SER	362	35.452	31.925	15.318	1.00	18.18	B1
ATOM	2497	CH	SER	357	22.576	28.480	14.495	1.00	29.48	B1	ATOM	2548	CH	SER	362	35.452	31.925	15.318	1.00	18.18	B1
ATOM	2498	CH	SER	357	22.576	28.480	14.495	1.00	29.48	B1	ATOM	2549	CH	SER	362	35.452	31.925	15.318	1.00	18.18	B1
ATOM	2499	CH	SER	357	22.576	28.480	14.495	1.00	29.48	B1	ATOM	2550	CH	SER	362	35.452	31.925	15.318	1.00	18.18	B1
ATOM	2500	CH	SER	357	22.576	28.480	14.495	1.00	29.48	B1	ATOM	2551	CH	SER	362	35.452	31.925	15.318	1.00	18.18	B1
ATOM	2501	CH	SER	357	22.576	28.480	14.495	1.00	29.48	B1	ATOM	2552	CH	SER	362	35.452	31.925	15.318	1.00	18.18	B1
ATOM	2502	CH	SER	357	22.576	28.480	14.495	1.00	29.48	B1	ATOM	2553	CH	SER	362	35.452	31.925	15.318	1.00	18.18	B1
ATOM	2503	CH	SER	357	22.576	28.480	14.495	1.00	29.48	B1	ATOM	2554	CH	SER	362	35.452	31.925	15.318	1.00	18.18	B1
ATOM	2504	CH	SER	357	22.576	28.480	14.495	1.00	29.48	B1	ATOM	2555	CH	SER	362	35.452	31.925	15.318	1.00	18.18	B1
ATOM	2505	CH	SER	357	22.576	28.480	14.495	1.00	29.48	B1	ATOM	2556	CH	SER	362	35.452	31.925	15.318	1.00	18.18	B1
ATOM	2506	CH	SER	357	22.576	28.480	14.495	1.00	29.48	B1	ATOM	2557	CH	SER	362	35.452	31.925	15.318	1.00	18.18	B1
ATOM	2507	CH	SER	357	22.576	28.480	14.495	1.00	29.48	B1	ATOM	2558	CH	SER	362	35.452	31.925	15.318	1.00	18.18	B1
ATOM	2508	CH	SER	357	22.576	28.480	14.495	1.00	29.48	B1	ATOM	2559	CH	SER	362	35.452	31.925	15.318	1.00	18.18	B1
ATOM	2509	CH	SER	357	22.576	28.480	14.495	1.00	29.48	B1	ATOM	2560	CH	SER	362	35.452	31.925	15.318	1.00	18.18	B1
ATOM	2510	CH	SER	357	22.576	28.480	14.495	1.00	29.48	B1	ATOM	2561	CH	SER	362	35.452	31.925	15.318	1.00	18.18	B1
ATOM	2511	CH	SER	357	22.576	28.480	14.495	1.00	29.48	B1	ATOM	2562	CH	SER	362	35.452	31.925	15.318	1.00	18.18	B1
ATOM	25																				

FIGURE 5

ATOM 2549 H	GLU 363	31.009	35.066	14.495	1.00	0.00	B1
ATOM 2550 C	GLU 363	33.496	37.090	14.145	1.00	30.30	B3
ATOM 2551 CG	GLU 363	31.763	36.235	11.849	1.00	30.90	B3
ATOM 2552 CG	GLU 363	31.763	36.235	11.849	1.00	30.90	B3
ATOM 2553 CD	GLU 363	33.642	37.663	11.013	1.00	42.62	B3
ATOM 2554 OE1	GLU 363	33.896	37.282	8.860	1.00	46.58	B3
ATOM 2555 OE2	GLU 363	33.896	37.282	8.860	1.00	46.58	B3
ATOM 2556 C	GLU 363	33.279	38.058	15.144	1.00	46.47	B3
ATOM 2557 O	GLU 363	33.837	37.726	15.239	1.00	36.16	B3
ATOM 2558 N	VAL 364	31.397	37.726	16.217	1.00	30.04	B3
ATOM 2559 CA	VAL 364	31.397	37.726	16.217	1.00	30.04	B3
ATOM 2560 CB	VAL 364	31.178	38.072	17.400	1.00	31.90	B3
ATOM 2561 CH	VAL 364	31.014	38.021	18.269	1.00	31.41	B3
ATOM 2562 CG1	VAL 364	30.860	38.811	15.562	1.00	30.73	B3
ATOM 2563 CG2	VAL 364	30.860	38.811	15.562	1.00	30.73	B3
ATOM 2564 C	VAL 364	33.642	37.282	11.013	1.00	42.62	B3
ATOM 2565 O	VAL 364	33.896	37.282	8.860	1.00	46.58	B3
ATOM 2566 CA	SEB 365	33.337	37.078	19.375	1.00	39.61	B3
ATOM 2567 CB	SEB 365	36.041	36.133	19.355	1.00	43.00	B3
ATOM 2568 CD	SEB 365	33.337	37.078	19.375	1.00	39.61	B3
ATOM 2569 CE	SEB 365	33.337	37.078	19.375	1.00	39.61	B3
ATOM 2570 CG	SEB 365	34.270	35.189	19.649	1.00	42.29	B3
ATOM 2571 CH	SEB 365	34.270	35.189	19.649	1.00	42.29	B3
ATOM 2572 C	SEB 365	36.398	38.418	18.840	1.00	38.21	B3
ATOM 2573 O	SEB 365	37.103	38.989	19.662	1.00	36.91	B3
ATOM 2574 CA	TYR 366	37.584	39.463	16.969	1.00	39.85	B3
ATOM 2575 N	TYR 366	36.075	37.945	16.910	1.00	0.00	B3
ATOM 2576 C	TYR 366	37.584	39.463	16.969	1.00	39.85	B3
ATOM 2577 CG	TYR 366	38.104	40.447	14.879	1.00	38.21	B3
ATOM 2578 CG	TYR 366	38.104	40.447	14.879	1.00	38.21	B3
ATOM 2579 CD	TYR 366	38.918	42.495	13.678	1.00	41.77	B3
ATOM 2580 CE	TYR 366	38.918	42.495	13.678	1.00	41.77	B3
ATOM 2581 C	TYR 366	40.849	41.466	14.739	1.00	40.76	B3
ATOM 2582 CD	TYR 366	40.849	41.466	14.739	1.00	40.76	B3
ATOM 2583 O	TYR 366	40.297	42.004	13.976	1.00	42.82	B3
ATOM 2584 OH	TYR 366	40.151	43.232	13.493	1.00	41.30	B3
ATOM 2585 N	TYR 366	37.133	40.893	17.241	1.00	40.55	B3
ATOM 2586 C	TYR 366	37.917	41.647	17.798	1.00	40.91	B3
ATOM 2587 O	TYR 366	37.917	41.647	17.798	1.00	40.91	B3
ATOM 2588 N	ARG 367	35.360	40.862	16.360	1.00	0.00	B3
ATOM 2589 CA	ARG 367	35.360	40.862	16.360	1.00	0.00	B3
ATOM 2590 CB	ARG 367	35.442	42.653	17.139	1.00	43.32	B3
ATOM 2591 CG	ARG 367	35.442	42.653	17.139	1.00	43.32	B3
ATOM 2592 CD	ARG 367	37.069	44.162	16.244	1.00	61.81	B3
ATOM 2593 CE	ARG 367	37.069	44.162	16.244	1.00	61.81	B3
ATOM 2594 NE	ARG 367	31.723	43.687	16.279	1.00	66.59	B3
ATOM 2595 HE	ARG 367	30.451	46.093	16.107	1.00	60.75	B3
ATOM 2596 H	ARG 367	30.451	46.093	16.107	1.00	60.75	B3
ATOM 2597 NH1	ARG 367	29.448	45.220	16.413	1.00	72.65	B3
ATOM 2598 NH2	ARG 367	29.431	42.236	16.410	1.00	0.00	B3
ATOM 2599 NH3	ARG 367	28.363	42.538	16.449	1.00	0.00	B3
ATOM 2600 NH4	ARG 367	28.363	42.538	16.449	1.00	0.00	B3
ATOM 2601 NH5	ARG 367	28.363	42.538	16.449	1.00	0.00	B3
ATOM 2602 NH6	ARG 367	28.363	42.538	16.449	1.00	0.00	B3
ATOM 2603 NH7	ARG 367	28.363	42.538	16.449	1.00	0.00	B3
ATOM 2604 O	ARG 367	35.531	43.011	15.615	1.00	40.10	B3
ATOM 2605 N	ARG 367	35.162	42.155	15.571	1.00	40.10	B3
ATOM 2606 H	ARG 367	35.162	42.155	15.571	1.00	40.10	B3
ATOM 2607 CA	VAL 368	34.726	41.316	19.217	1.00	19.91	B3
ATOM 2608 CB	VAL 368	35.331	42.792	20.908	1.00	17.33	B3
ATOM 2609 CG	VAL 368	35.331	42.792	20.908	1.00	17.33	B3
ATOM 2610 CH	VAL 368	35.007	40.867	22.584	1.00	15.03	B3
ATOM 2611 O	VAL 368	33.259	41.230	21.584	1.00	35.49	B3
ATOM 2612 O	VAL 368	33.259	41.230	21.584	1.00	35.49	B3
ATOM 2613 N	LEU 369	37.492	40.818	20.308	1.00	0.00	B3
ATOM 2614 CA	LEU 369	37.492	40.818	20.308	1.00	0.00	B3
ATOM 2615 CB	LEU 369	39.884	40.601	20.679	1.00	21.15	B3
ATOM 2616 CH	LEU 369	39.884	40.601	20.679	1.00	21.15	B3
ATOM 2617 CG	LEU 369	39.817	43.011	20.542	1.00	41.98	B3
ATOM 2618 CD	LEU 369	40.711	43.654	21.144	1.00	41.30	B3
ATOM 2619 CE	LEU 369	40.711	43.654	21.144	1.00	41.30	B3
ATOM 2620 C	LEU 369	39.819	44.577	18.864	1.00	45.96	B3
ATOM 2621 O	LEU 369	39.819	44.577	18.864	1.00	45.96	B3
ATOM 2622 O	LEU 369	39.819	44.577	18.864	1.00	45.96	B3
ATOM 2623 H	ARG 370	39.124	45.779	16.136	1.00	47.06	B3
ATOM 2624 CA	ARG 370	39.124	45.779	16.136	1.00	47.06	B3
ATOM 2625 CB	ARG 370	40.984	45.910	16.169	1.00	45.37	B3
ATOM 2626 CD	ARG 370	40.984	45.910	16.169	1.00	45.37	B3
ATOM 2627 CE	ARG 370	41.219	46.681	14.976	1.00	46.00	B3
ATOM 2628 NE	ARG 370	41.219	46.681	14.976	1.00	46.00	B3
ATOM 2629 H	ARG 370	41.219	46.681	14.976	1.00	46.00	B3
ATOM 2630 C	ARG 370	42.469	47.153	14.291	1.00	48.45	B3
ATOM 2631 NH1	ARG 370	43.443	46.961	15.607	1.00	70.13	B3
ATOM 2632 NH2	ARG 370	43.443	46.961	15.607	1.00	70.13	B3
ATOM 2633 NH3	ARG 370	43.443	46.961	15.607	1.00	70.13	B3
ATOM 2634 NH4	ARG 370	43.443	46.961	15.607	1.00	70.13	B3
ATOM 2635 NH5	ARG 370	43.443	46.961	15.607	1.00	70.13	B3
ATOM 2636 NH6	ARG 370	43.443	46.961	15.607	1.00	70.13	B3
ATOM 2637 C	ARG 370	39.386	45.740	19.538	1.00	49.17	B3
ATOM 2638 O	ARG 370	40.216	46.615	19.816	1.00	49.84	B3
ATOM 2639 H	ARG 370	40.216	46.615	19.816	1.00	49.84	B3
ATOM 2640 H	ARG 370	37.581	44.755	19.945	1.00	51.00	B3
ATOM 2641 CA	HIS 371	37.455	46.718	21.080	1.00	56.65	B3
ATOM 2642 CB	HIS 371	37.455	46.718	21.080	1.00	56.65	B3
ATOM 2643 CD	HIS 371	35.596	47.877	19.313	1.00	75.03	B3
ATOM 2644 CE	HIS 371	35.596	47.877	19.313	1.00	75.03	B3
ATOM 2645 ND1	HIS 371	34.067	46.346	20.106	1.00	75.01	B3
ATOM 2646 ND2	HIS 371	34.067	46.346	20.106	1.00	75.01	B3
ATOM 2647 CE1	HIS 371	33.500	47.116	19.077	1.00	70.71	B3
ATOM 2648 CE2	HIS 371	34.507	47.914	18.573	1.00	77.52	B3
ATOM 2649 NE2	HIS 371	34.507	47.914	18.573	1.00	77.52	B3
ATOM 2650 C	HIS 371	38.551	49.069	22.049	1.00	76.70	B3

FIGURE 5

ATOM 2651 O H5 371	38.458	47.592	23.176	1.00	58.12	83
ATOM 2652 H LEU 372	37.910	45.837	22.715	1.00	56.98	83
ATOM 2653 H LEU 372	39.100	46.048	45.597	2.6939	1.00	57.77
ATOM 2654 CA LEU 372	38.715	44.772	24.633	1.00	51.29	83
ATOM 2655 CB LEU 372	37.975	44.772	24.633	1.00	51.29	83
ATOM 2656 CD LEU 372	38.315	44.899	23.176	1.00	55.87	83
ATOM 2657 CD LEU 372	38.315	44.899	23.176	1.00	55.87	83
ATOM 2658 CD LEU 372	38.315	44.899	23.176	1.00	55.87	83
ATOM 2659 N LEU 372	41.554	45.155	23.647	1.00	58.81	83
ATOM 2660 N LEU 372	41.554	45.155	23.647	1.00	58.81	83
ATOM 2661 N LEU 372	41.592	46.168	22.447	1.00	59.37	83
ATOM 2662 H ALA 373	41.271	46.155	21.731	1.00	60.03	83
ATOM 2663 H ALA 373	41.271	46.155	21.731	1.00	60.03	83
ATOM 2664 CA ALA 373	43.179	47.955	21.762	1.00	61.21	83
ATOM 2665 CA ALA 373	43.166	47.955	21.762	1.00	61.21	83
ATOM 2666 OTI ALA 373	44.798	48.243	21.697	1.00	62.45	83
ATOM 2667 H LEU 410	23.074	47.596	-0.330	1.00	52.64	83
ATOM 2670 CD LEU 410	23.074	47.596	-0.330	1.00	52.64	83
ATOM 2671 CD LEU 410	23.074	47.596	-0.330	1.00	52.64	83
ATOM 2672 N LEU 410	23.982	47.412	0.718	1.00	51.85	83
ATOM 2673 O LEU 410	23.982	47.412	0.718	1.00	51.85	83
ATOM 2674 H LEU 410	22.841	47.124	1.635	1.00	52.98	83
ATOM 2675 H LEU 410	22.841	47.124	1.635	1.00	52.98	83
ATOM 2676 N LEU 410	22.198	49.563	-0.415	1.00	54.31	83
ATOM 2677 H LEU 410	22.359	49.517	-0.598	1.00	54.31	83
ATOM 2678 N LEU 410	22.450	51.413	2.965	1.00	52.95	83
ATOM 2679 N LEU 410	22.450	51.413	2.965	1.00	52.95	83
ATOM 2680 CD PRO 411	22.466	50.407	4.072	1.00	52.54	83
ATOM 2681 CA PRO 411	22.466	50.407	4.072	1.00	52.54	83
ATOM 2682 CA PRO 411	22.466	50.407	4.072	1.00	52.54	83
ATOM 2683 CG PRO 411	23.163	51.108	5.203	1.00	52.83	83
ATOM 2684 N PRO 411	23.958	53.413	3.021	1.00	53.47	83
ATOM 2685 N PRO 411	23.958	53.413	3.021	1.00	53.47	83
ATOM 2686 N PRO 411	23.958	53.413	3.021	1.00	53.47	83
ATOM 2687 H GLN 412	22.863	54.500	2.794	1.00	50.00	83
ATOM 2688 CA GLN 412	24.873	55.413	1.871	1.00	50.44	83
ATOM 2689 CG GLN 412	25.364	57.408	0.437	1.00	56.51	83
ATOM 2690 CG GLN 412	25.364	57.408	0.437	1.00	56.51	83
ATOM 2691 CD GLN 412	25.328	56.954	-1.017	1.00	55.40	83
ATOM 2692 CD GLN 412	25.328	56.954	-1.017	1.00	55.40	83
ATOM 2693 CD GLN 412	25.328	56.954	-1.017	1.00	55.40	83
ATOM 2694 NE2 GLN 412	23.714	55.616	-0.737	1.00	60.00	83
ATOM 2695 NE2 GLN 412	23.714	55.616	-0.737	1.00	60.00	83
ATOM 2696 N SER 413	25.614	55.842	4.201	1.00	47.90	83
ATOM 2697 O GLN 412	27.089	55.591	2.545	1.00	46.78	83
ATOM 2698 N SER 413	25.614	55.842	4.201	1.00	47.90	83
ATOM 2699 H SER 413	24.609	55.984	5.164	1.00	48.25	83
ATOM 2700 H SER 413	24.609	55.984	5.164	1.00	48.25	83
ATOM 2701 CD SER 413	26.261	56.344	6.548	1.00	50.61	83
ATOM 2702 OG SER 413	27.378	56.877	7.401	1.00	51.08	83
ATOM 2703 HG SER 413	28.178	56.315	7.401	1.00	51.08	83
ATOM 2704 C SER 413	27.490	54.684	5.267	1.00	48.21	83
ATOM 2705 N PHE 414	26.898	54.839	5.332	1.00	50.71	83
ATOM 2706 N PHE 414	26.898	54.839	5.332	1.00	50.71	83
ATOM 2707 H PHE 414	25.996	53.245	5.015	1.00	51.00	83
ATOM 2708 H PHE 414	27.787	53.245	5.015	1.00	51.00	83
ATOM 2709 CA PHE 414	26.958	50.575	5.212	1.00	46.76	83
ATOM 2710 CG PHE 414	27.883	49.256	5.425	1.00	46.71	83
ATOM 2711 CD PHE 414	28.782	48.000	5.663	1.00	44.81	83
ATOM 2712 CE1 PHE 414	28.782	48.000	5.663	1.00	44.81	83
ATOM 2713 CE2 PHE 414	28.832	47.402	5.247	1.00	43.40	83
ATOM 2714 CE3 PHE 414	28.781	47.223	3.923	1.00	44.42	83
ATOM 2715 C PHE 414	28.122	52.748	2.942	1.00	43.50	83
ATOM 2716 N LEU 415	29.831	51.903	4.310	1.00	41.22	83
ATOM 2717 O PHE 414	29.831	51.903	4.310	1.00	41.22	83
ATOM 2718 N LEU 415	27.188	53.144	2.946	1.00	43.00	83
ATOM 2719 O PHE 414	27.188	53.144	2.946	1.00	43.00	83
ATOM 2720 CA LEU 415	27.946	53.205	0.641	1.00	41.78	83
ATOM 2721 CB LEU 415	27.946	53.205	0.641	1.00	41.78	83
ATOM 2722 CD LEU 415	27.946	53.205	0.641	1.00	41.78	83
ATOM 2723 N LEU 415	30.081	53.669	1.755	1.00	40.63	83
ATOM 2724 CD LEU 415	30.081	53.669	1.755	1.00	40.63	83
ATOM 2725 C LEU 415	29.940	54.779	2.183	1.00	40.28	83
ATOM 2726 N LEU 415	29.940	54.779	2.183	1.00	40.28	83
ATOM 2727 H LEU 415	29.028	54.548	2.899	1.00	41.00	83
ATOM 2728 H LEU 415	29.028	54.548	2.899	1.00	41.00	83
ATOM 2729 CA LEU 416	29.438	37.704	1.851	1.00	55.24	83
ATOM 2730 CB LEU 416	31.957	33.338	3.366	1.00	55.30	83
ATOM 2731 CG LEU 416	31.957	33.338	3.366	1.00	55.30	83
ATOM 2732 CD LEU 416	31.957	33.338	3.366	1.00	55.30	83
ATOM 2733 N LEU 416	31.853	53.087	6.600	1.00	45.31	83
ATOM 2734 C LEU 416	31.853	53.087	6.600	1.00	45.31	83
ATOM 2735 O LEU 416	31.131	55.427	3.270	1.00	53.12	83
ATOM 2736 H ALA 417	31.573	54.619	4.655	1.00	47.05	83
ATOM 2737 H ALA 417	31.573	54.619	4.655	1.00	47.05	83
ATOM 2738 CA ALA 417	31.573	54.619	4.655	1.00	47.05	83
ATOM 2739 CB ALA 417	31.573	54.619	4.655	1.00	47.05	83
ATOM 2740 CG ALA 417	31.573	54.619	4.655	1.00	47.05	83
ATOM 2741 N ALA 417	31.573	54.619	4.655	1.00	47.05	83
ATOM 2742 N CYS 418	31.573	54.619	4.655	1.00	47.05	83
ATOM 2743 CYS 418	31.573	54.619	4.655	1.00	47.05	83
ATOM 2744 CYS 418	31.573	54.619	4.655	1.00	47.05	83
ATOM 2745 CB CYS 418	31.573	54.619	4.655	1.00	47.05	83
ATOM 2746 CG CYS 418	31.573	54.619	4.655	1.00	47.05	83
ATOM 2747 N LEU 419	31.573	54.619	4.655	1.00	47.05	83
ATOM 2748 O CYS 418	31.573	54.619	4.655	1.00	47.05	83
ATOM 2749 N LEU 419	31.573	54.619	4.655	1.00	47.05	83
ATOM 2750 N LEU 419	31.573	54.619	4.655	1.00	47.05	83
ATOM 2751 CA LEU 419	31.573	54.619	4.655	1.00	47.05	83
ATOM 2752 N LEU 419	31.573	54.619	4.655	1.00	47.05	83

FIGURE 5

ATOM 2753 C	LEH	419	32.866	53.853	-12.344	1.00	10.641	C1
ATOM 2754 CD	LEH	419	31.806	54.918	-1.609	1.00	10.934	C1
ATOM 2755 CD	LEH	419	33.349	52.027	-2.553	1.00	10.924	C1
ATOM 2756 N	LEH	419	37.198	53.971	0.549	1.00	10.733	C1
ATOM 2757 O	LEH	419	35.974	54.483	2.773	1.00	11.129	C1
ATOM 2758 N	GILU	420	35.068	54.578	1.648	1.00	10.000	C1
ATOM 2759 N	GILU	420	36.477	55.462	4.194	1.00	10.279	C1
ATOM 2760 C	GILU	420	36.477	55.462	4.194	1.00	10.279	C1
ATOM 2761 C	GILU	420	37.420	56.740	5.185	1.00	10.366	C1
ATOM 2762 CG	GILU	420	35.957	56.499	6.009	1.00	10.430	C1
ATOM 2763 CD	GILU	420	35.957	56.499	6.009	1.00	10.430	C1
ATOM 2764 OEG	GILU	420	35.743	56.345	6.954	1.00	10.421	C1
ATOM 2765 OEG	GILU	420	35.743	56.345	6.954	1.00	10.421	C1
ATOM 2766 N	GILU	421	36.843	53.763	3.423	1.00	11.147	C1
ATOM 2767 N	GILU	421	38.466	51.461	4.283	1.00	10.734	C1
ATOM 2768 N	GILU	421	37.533	52.454	3.970	1.00	10.346	C1
ATOM 2769 H	GILU	421	36.883	53.556	4.098	1.00	10.000	C1
ATOM 2770 C	GILU	421	38.466	51.461	4.283	1.00	10.734	C1
ATOM 2771 CD	GILU	421	35.357	49.236	6.394	1.00	10.418	C1
ATOM 2772 CD	GILU	421	35.357	49.236	6.394	1.00	10.418	C1
ATOM 2773 CG	GILU	421	37.408	50.634	6.463	1.00	10.318	C1
ATOM 2774 CD	GILU	421	36.320	49.635	7.058	1.00	10.749	C1
ATOM 2775 NE1	GILU	421	35.357	49.236	6.394	1.00	10.418	C1
ATOM 2776 NE2	GILU	421	35.695	48.305	8.156	1.00	10.000	C1
ATOM 2777 NE3	GILU	421	37.207	49.330	8.817	1.00	10.000	C1
ATOM 2778 N	GILU	421	40.133	50.445	1.099	1.00	10.709	C1
ATOM 2779 O	GILU	421	40.133	50.445	1.099	1.00	10.709	C1
ATOM 2780 N	VAL	422	38.379	50.845	1.847	1.00	10.237	C1
ATOM 2781 N	VAL	422	38.379	50.845	1.847	1.00	10.237	C1
ATOM 2782 C	VAL	422	39.077	50.420	0.561	1.00	10.253	C1
ATOM 2783 C	VAL	422	38.163	50.636	0.556	1.00	10.267	C1
ATOM 2784 CG	VAL	422	38.875	50.455	-1.164	1.00	11.536	C1
ATOM 2785 CG	VAL	422	38.875	50.455	-1.164	1.00	11.536	C1
ATOM 2786 C	VAL	422	40.333	51.254	0.514	1.00	10.762	C1
ATOM 2787 O	VAL	422	41.458	50.708	0.508	1.00	10.277	C1
ATOM 2788 N	ARG	423	38.403	53.019	0.715	1.00	10.000	C1
ATOM 2789 C	ARG	423	41.438	53.456	0.346	1.00	10.259	C1
ATOM 2790 C	ARG	423	41.438	53.456	0.346	1.00	10.259	C1
ATOM 2791 C	ARG	423	39.707	55.387	3.216	1.00	10.318	C1
ATOM 2792 C	ARG	423	40.325	54.798	2.177	1.00	10.255	C1
ATOM 2793 NE	ARG	423	39.707	55.387	3.216	1.00	10.318	C1
ATOM 2794 NE	ARG	423	40.325	54.798	2.177	1.00	10.255	C1
ATOM 2795 C	ARG	423	39.707	55.387	3.216	1.00	10.318	C1
ATOM 2796 C	ARG	423	40.325	54.798	2.177	1.00	10.255	C1
ATOM 2797 NH1	ARG	423	40.264	53.857	-4.949	1.00	10.327	C1
ATOM 2798 NH11	ARG	423	40.264	53.857	-4.949	1.00	10.327	C1
ATOM 2799 NH1	ARG	423	40.264	53.857	-4.949	1.00	10.327	C1
ATOM 2800 NH2	ARG	423	38.960	55.882	-5.325	1.00	10.318	C1
ATOM 2801 NH21	ARG	423	38.960	55.882	-5.325	1.00	10.318	C1
ATOM 2802 NH2	ARG	423	38.960	55.882	-5.325	1.00	10.318	C1
ATOM 2803 C	ARG	423	41.219	53.241	-4.427	1.00	10.260	C1
ATOM 2804 C	ARG	423	41.219	53.241	-4.427	1.00	10.260	C1
ATOM 2805 O	ARG	423	43.594	53.147	1.127	1.00	10.243	C1
ATOM 2806 H	ARG	423	41.109	53.051	2.506	1.00	10.248	C1
ATOM 2807 CA	ARG	424	41.064	53.855	3.773	1.00	10.2512	C1
ATOM 2808 CG	ARG	424	41.323	52.791	5.051	1.00	10.289	C1
ATOM 2809 CG	ARG	424	41.323	52.791	5.051	1.00	10.289	C1
ATOM 2810 CD	ARG	424	41.579	52.380	7.466	1.00	10.553	C1
ATOM 2811 CE	ARG	424	41.238	53.425	7.853	1.00	10.453	C1
ATOM 2812 CE	ARG	424	41.238	53.425	7.853	1.00	10.453	C1
ATOM 2813 NE1	ARG	424	41.079	53.555	7.055	1.00	10.423	C1
ATOM 2814 NE2	ARG	424	40.708	53.136	7.065	1.00	10.000	C1
ATOM 2815 C	ARG	424	40.708	53.136	7.065	1.00	10.000	C1
ATOM 2816 C	ARG	424	40.708	53.136	7.065	1.00	10.000	C1
ATOM 2817 O	ARG	424	40.923	53.425	3.448	1.00	10.504	C1
ATOM 2818 N	ARG	425	41.190	50.542	2.794	1.00	10.263	C1
ATOM 2819 N	ARG	425	41.190	50.542	2.794	1.00	10.263	C1
ATOM 2820 CA	ARG	425	41.969	49.317	2.561	1.00	10.516	C1
ATOM 2821 CB	ARG	425	41.965	48.093	2.336	1.00	10.491	C1
ATOM 2822 CG	ARG	425	41.854	46.786	1.975	1.00	10.231	C1
ATOM 2823 CG	ARG	425	41.854	46.786	1.975	1.00	10.231	C1
ATOM 2824 CD	ARG	425	40.885	47.169	3.432	1.00	10.568	C1
ATOM 2825 C	ARG	425	44.824	49.549	1.346	1.00	10.284	C1
ATOM 2826 C	ARG	425	44.824	49.549	1.346	1.00	10.284	C1
ATOM 2827 N	GILU	426	41.381	50.607	0.214	1.00	10.424	C1
ATOM 2828 H	GILU	426	41.451	50.620	0.193	1.00	10.000	C1
ATOM 2829 C	GILU	426	44.431	51.244	-1.896	1.00	10.264	C1
ATOM 2830 CG	GILU	426	43.715	50.539	-1.996	1.00	11.536	C1
ATOM 2831 CG	GILU	426	43.715	50.539	-1.996	1.00	11.536	C1
ATOM 2832 CG	GILU	426	42.786	51.047	-3.151	1.00	10.252	C1
ATOM 2833 CG	GILU	426	42.786	51.047	-3.151	1.00	10.252	C1
ATOM 2834 NE2	GILU	426	42.337	50.509	-4.672	1.00	10.255	C1
ATOM 2835 NE3	GILU	426	41.755	50.948	-5.333	1.00	10.000	C1
ATOM 2837 C	GILU	426	46.404	51.312	-0.488	1.00	10.269	C1
ATOM 2838 O	GILU	426	47.466	51.109	-1.046	1.00	10.273	C1
ATOM 2839 N	GILU	426	45.403	51.114	0.855	1.00	10.000	C1
ATOM 2840 H	GILU	427	45.410	51.114	0.855	1.00	10.000	C1
ATOM 2841 CA	GILU	427	47.446	52.894	1.012	1.00	10.245	C1
ATOM 2842 C	GILU	427	48.567	51.791	1.366	1.00	10.208	C1
ATOM 2843 C	GILU	427	48.567	51.791	1.366	1.00	10.208	C1
ATOM 2844 N	ASP	428	48.107	51.073	2.575	1.00	10.275	C1
ATOM 2845 H	ASP	428	47.189	51.111	2.718	1.00	10.000	C1
ATOM 2846 H	ASP	428	47.189	51.111	2.718	1.00	10.000	C1
ATOM 2847 CG	ASP	428	48.415	49.199	4.111	1.00	10.263	C1
ATOM 2848 CG	ASP	428	47.437	49.779	5.097	1.00	10.284	C1
ATOM 2849 CG	ASP	428	47.437	49.779	5.097	1.00	10.284	C1
ATOM 2850 OEG	ASP	428	48.642	50.804	5.176	1.00	10.307	C1
ATOM 2851 C	ASP	428	49.626	49.191	2.063	1.00	10.243	C1
ATOM 2852 O	ASP	428	48.840	48.422	1.909	1.00	10.000	C1
ATOM 2853 H	ASP	429	47.905	49.113	1.071	1.00	10.000	C1
ATOM 2854 H	ASP	429	47.905	49.113	1.071	1.00	10.000	C1

ATOM	2855	C	GLV	479	49	3819	47.9640	0.029	100.25	44	ATOM	2906	CE	LX5	435	58	3424	48.748	4.137	1.00	40.31	C1
ATOM	2856	C	GLV	479	50	4005	48.9690	-0.716	100.25	44	ATOM	2907	CE	LX5	435	59	3429	49.014	4.137	1.00	40.31	C1
ATOM	2857	C	GLV	479	51	4118	48.185	-0.171	100.78	51	ATOM	2908	CE	LX5	435	60	3434	49.281	4.137	1.00	40.31	C1
ATOM	2858	C	GLV	479	52	4216	48.305	-1.171	100.60	51	ATOM	2909	CE	LX5	435	61	3439	49.548	4.137	1.00	40.31	C1
ATOM	2859	H	ALA	430	49	34216	50.815	-1.727	100.10	43	ATOM	2910	CE	LX5	435	62	3444	49.815	4.137	1.00	40.31	C1
ATOM	2860	H	ALA	430	50	35094	50.637	-2.035	100.26	44	ATOM	2911	CE	LX5	435	63	3449	50.082	4.137	1.00	40.31	C1
ATOM	2861	H	ALA	430	51	35972	50.459	-2.343	100.42	44	ATOM	2912	CE	LX5	435	64	3454	50.349	4.137	1.00	40.31	C1
ATOM	2862	C	ALA	480	49	32300	50.617	-1.131	100.75	49	ATOM	2913	CE	LX5	435	65	3459	50.616	4.137	1.00	40.31	C1
ATOM	2863	C	ALA	480	50	33193	50.933	-1.665	100.25	43	ATOM	2914	CE	LX5	435	66	3464	50.883	4.137	1.00	40.31	C1
ATOM	2864	C	ALA	480	51	34176	51.079	-1.964	100.43	43	ATOM	2915	CE	LX5	435	67	3469	51.150	4.137	1.00	40.31	C1
ATOM	2865	C	ALA	480	52	35159	51.225	-2.262	100.59	43	ATOM	2916	CE	LX5	435	68	3474	51.417	4.137	1.00	40.31	C1
ATOM	2866	C	ALA	431	51	33274	51.372	2.458	100.74	49	ATOM	2917	CE	LX5	435	69	3479	51.684	4.137	1.00	40.31	C1
ATOM	2867	C	ALA	431	52	34257	51.519	2.756	100.90	49	ATOM	2918	CE	LX5	435	70	3484	51.951	4.137	1.00	40.31	C1
ATOM	2868	C	ALA	431	53	35140	51.666	3.053	100.31	47	ATOM	2919	CE	LX5	435	71	3489	52.218	4.137	1.00	40.31	C1
ATOM	2869	C	ALA	431	54	36023	51.813	3.351	100.47	47	ATOM	2920	CE	LX5	435	72	3494	52.485	4.137	1.00	40.31	C1
ATOM	2870	N	EBJ	431	43	33562	48.777	0.303	100.31	47	ATOM	2921	CE	LX5	435	73	3499	52.752	4.137	1.00	40.31	C1
ATOM	2871	N	EBJ	431	44	34445	48.924	0.601	100.47	47	ATOM	2922	CE	LX5	435	74	3504	53.019	4.137	1.00	40.31	C1
ATOM	2872	N	EBJ	431	45	35328	49.071	0.898	100.63	47	ATOM	2923	CE	LX5	435	75	3509	53.286	4.137	1.00	40.31	C1
ATOM	2873	C	EBJ	431	43	34310	48.615	1.301	100.37	41	ATOM	2924	CE	LX5	435	76	3514	53.553	4.137	1.00	40.31	C1
ATOM	2874	C	EBJ	431	44	35193	48.762	1.598	100.53	41	ATOM	2925	CE	LX5	435	77	3519	53.820	4.137	1.00	40.31	C1
ATOM	2875	C	EBJ	431	45	36076	48.909	1.896	100.69	41	ATOM	2926	CE	LX5	435	78	3524	54.087	4.137	1.00	40.31	C1
ATOM	2876	C	EBJ	431	46	36959	49.056	2.194	100.85	41	ATOM	2927	CE	LX5	435	79	3529	54.354	4.137	1.00	40.31	C1
ATOM	2877	C	EBJ	431	47	37842	49.203	2.492	101.01	41	ATOM	2928	CE	LX5	435	80	3534	54.621	4.137	1.00	40.31	C1
ATOM	2878	C	EBJ	431	48	38725	49.350	2.790	101.17	41	ATOM	2929	CE	LX5	435	81	3539	54.888	4.137	1.00	40.31	C1
ATOM	2879	C	EBJ	431	49	39608	49.497	3.088	101.33	41	ATOM	2930	CE	LX5	435	82	3544	55.155	4.137	1.00	40.31	C1
ATOM	2880	C	EBJ	431	50	40491	49.644	3.386	101.49	41	ATOM	2931	CE	LX5	435	83	3549	55.422	4.137	1.00	40.31	C1
ATOM	2881	C	EBJ	431	51	41374	49.791	3.684	101.65	41	ATOM	2932	CE	LX5	435	84	3554	55.689	4.137	1.00	40.31	C1
ATOM	2882	C	EBJ	431	52	42257	49.938	3.982	101.81	41	ATOM	2933	CE	LX5	435	85	3559	55.956	4.137	1.00	40.31	C1
ATOM	2883	C	EBJ	431	53	43140	50.085	4.280	101.97	41	ATOM	2934	CE	LX5	435	86	3564	56.223	4.137	1.00	40.31	C1
ATOM	2884	C	GLM	433	32	32049	47.991	-0.973	100.42	46	ATOM	2935	CE	LX5	435	87	3569	56.490	4.137	1.00	40.31	C1
ATOM	2885	C	GLM	433	33	32932	48.138	-1.271	100.58	46	ATOM	2936	CE	LX5	435	88	3574	56.757	4.137	1.00	40.31	C1
ATOM	2886	C	GLM	433	34	33815	48.285	-1.569	100.74	46	ATOM	2937	CE	LX5	435	89	3579	57.024	4.137	1.00	40.31	C1
ATOM	2887	C	GLM	433	35	34698	48.432	-1.867	100.90	46	ATOM	2938	CE	LX5	435	90	3584	57.291	4.137	1.00	40.31	C1
ATOM	2888	C	GLM	433	36	35581	48.579	-2.165	101.06	46	ATOM	2939	CE	LX5	435	91	3589	57.558	4.137	1.00	40.31	C1
ATOM	2889	C	GLM	433	37	36464	48.726	-2.463	101.22	46	ATOM	2940	CE	LX5	435	92	3594	57.825	4.137	1.00	40.31	C1
ATOM	2890	C	GLN	433	32	32948	48.003	-0.973	100.42	46	ATOM	2941	CE	LX5	435	93	3599	58.092	4.137	1.00	40.31	C1
ATOM	2891	C	GLN	433	33	33831	48.150	-1.271	100.58	46	ATOM	2942	CE	LX5	435	94	3604	58.359	4.137	1.00	40.31	C1
ATOM	2892	C	GLN	433	34	34714	48.297	-1.569	100.74	46	ATOM	2943	CE	LX5	435	95	3609	58.626	4.137	1.00	40.31	C1
ATOM	2893	C	GLN	433	35	35597	48.444	-1.867	100.90	46	ATOM	2944	CE	LX5	435	96	3614	58.893	4.137	1.00	40.31	C1
ATOM	2894	C	GLN	433	36	36480	48.591	-2.165	101.06	46	ATOM	2945	CE	LX5	435	97	3619	59.160	4.137	1.00	40.31	C1
ATOM	2895	C	GLN	433	37	37363	48.738	-2.463	101.22	46	ATOM	2946	CE	LX5	435	98	3624	59.427	4.137	1.00	40.31	C1
ATOM	2896	C	GLN	433	38	38246	48.885	-2.761	101.38	46	ATOM	2947	CE	LX5	435	99	3629	59.694	4.137	1.00	40.31	C1
ATOM	2897	C	GLU	434	32	32992	48.030	-0.973	100.42	46	ATOM	2948	CE	LX5	435	100	3634	59.961	4.137	1.00	40.31	C1
ATOM	2898	C	GLU	434	33	33875	48.177	-1.271	100.58	46	ATOM	2949	CE	LX5	435	101	3639	60.228	4.137	1.00	40.31	C1
ATOM	2899	C	GLU	434	34	34758	48.324	-1.569	100.74	46	ATOM	2950	CE	LX5	435	102	3644	60.495	4.137	1.00	40.31	C1
ATOM	2900	C	GLU	434	35	35641	48.471	-1.867	100.90	46	ATOM	2951	CE	LX5	435	103	3649	60.762	4.137	1.00	40.31	C1
ATOM	2901	C	GLU	434	36	36524	48.618	-2.165	101.06	46	ATOM	2952	CE	LX5	435	104	3654	61.029	4.137	1.00	40.31	C1
ATOM	2902	C	GLU	434	37	37407	48.765	-2.463	101.22	46	ATOM	2953	CE	LX5	435	105	3659	61.296	4.137	1.00	40.31	C1
ATOM	2903	C	GLU	434	38	38290	48.912	-2.761	101.38	46	ATOM	2954	CE	LX5	435	106	3664	61.563	4.137	1.00	40.31	C1
ATOM	2904	C	GLU	434	39	39173	49.059	-3.059	101.54	46	ATOM	2955	CE	LX5	435	107	3669	61.830	4.137	1.00	40.31	C1
ATOM	2905	C	GLU	434	40	40056	49.206	-3.357	101.70	46	ATOM	2956	CE	LX5	435	108	3674	62.097	4.137	1.00	40.31	C1

FIGURE 5

ATOM 2957 C T1R 440	65.088	44.768	-3.681	1.00	3.407	C1
ATOM 2958 O T1R 440	65.598	43.823	-4.267	1.00	3.554	C1
ATOM 2960 H T1R 440	64.637	45.821	-4.330	1.00	3.318	C1
ATOM 2961 CA T1S 441	64.395	45.957	-5.763	1.00	3.044	C1
ATOM 2962 CB T1S 441	65.983	45.759	-5.364	1.00	3.276	C1
ATOM 2963 CD T1S 441	67.725	47.000	-5.607	1.00	3.959	C1
ATOM 2964 CE T1S 441	67.725	47.000	-5.607	1.00	3.959	C1
ATOM 2965 CF T1S 441	67.503	49.021	-6.984	1.00	5.137	C1
ATOM 2966 CG T1S 441	66.367	49.780	-7.240	1.00	5.764	C1
ATOM 2967 CH T1S 441	65.885	49.325	-4.173	1.00	1.000	C1
ATOM 2968 HI2 T1S 441	65.885	49.325	-4.173	1.00	1.000	C1
ATOM 2969 HI3 T1S 441	66.468	50.801	-5.219	1.00	0.000	C1
ATOM 2970 C T1S 441	63.639	45.015	-6.425	1.00	2.846	C1
ATOM 2971 N T1S 441	62.332	44.924	-4.837	1.00	0.000	C1
ATOM 2972 H T1S 441	62.332	44.924	-4.837	1.00	0.000	C1
ATOM 2973 H T1S 441	62.332	44.924	-4.837	1.00	0.000	C1
ATOM 2974 H T1S 441	62.332	44.924	-4.837	1.00	0.000	C1
ATOM 2975 CB T1S 441	61.905	41.634	-4.847	1.00	2.775	C1
ATOM 2976 CG T1S 441	61.905	41.634	-4.847	1.00	2.775	C1
ATOM 2977 CD T1S 441	61.905	41.634	-4.847	1.00	2.775	C1
ATOM 2978 CE T1S 441	61.905	41.634	-4.847	1.00	2.775	C1
ATOM 2979 C T1S 441	60.575	44.892	-6.635	1.00	3.659	C1
ATOM 2980 O T1S 441	59.811	45.261	-5.741	1.00	3.236	C1
ATOM 2981 H T1S 441	61.423	45.199	-4.389	1.00	0.000	C1
ATOM 2982 H T1S 441	61.423	45.199	-4.389	1.00	0.000	C1
ATOM 2983 CA T1S 441	59.866	46.645	-4.191	1.00	3.269	C1
ATOM 2984 C T1S 441	58.807	46.310	-5.217	1.00	3.143	C1
ATOM 2985 CB T1S 441	60.715	47.800	-6.743	1.00	3.674	C1
ATOM 2986 CG T1S 441	61.938	48.345	-7.519	1.00	3.746	C1
ATOM 2987 CH T1S 441	61.938	48.345	-7.519	1.00	3.746	C1
ATOM 2988 HI1 T1S 441	55.697	44.460	-9.959	1.00	0.000	C1
ATOM 2989 CA T1S 441	57.662	45.173	-10.975	1.00	3.775	C1
ATOM 2991 CB T1S 441	58.359	45.374	-12.310	1.00	3.709	C1
ATOM 2992 CD T1S 441	60.314	46.664	-12.075	1.00	4.140	C1
ATOM 2993 CE T1S 441	58.811	47.563	-13.261	1.00	4.174	C1
ATOM 2994 HI1 T1S 441	59.815	48.372	-13.317	1.00	4.200	C1
ATOM 2995 CB T1S 441	60.817	47.843	-12.302	1.00	4.138	C1
ATOM 2996 CG T1S 441	61.990	48.748	-12.334	1.00	4.000	C1
ATOM 2997 HI2 T1S 441	57.461	41.867	-11.309	1.00	4.015	C1
ATOM 2998 HI3 T1S 441	55.615	43.753	-10.406	1.00	4.066	C1
ATOM 3001 N T1S 441	54.313	42.497	-10.716	1.00	4.030	C1
ATOM 3002 C T1S 441	53.669	42.872	-9.730	1.00	3.935	C1
ATOM 3003 CG T1S 441	53.669	42.872	-9.730	1.00	3.935	C1
ATOM 3004 CH T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3005 O T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3006 H T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3007 C T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3008 N T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3009 CA T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3010 CB T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3011 CD T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3012 CE T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3013 CH T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3014 OI1 T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3015 OI2 T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3016 OI3 T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3017 O T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3018 N T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3019 CA T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3020 CB T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3021 CD T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3022 CE T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3023 CH T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3024 OI1 T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3025 OI2 T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3026 OI3 T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3027 O T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3028 N T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3029 CA T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3030 CB T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3031 CD T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3032 CE T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3033 CH T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3034 OI1 T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3035 C T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3036 N T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3037 H T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3038 H T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3039 CA T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3040 CB T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3041 CG T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3042 CH T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3043 OI1 T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3044 C T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3045 N T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3046 H T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3047 CA T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3048 CB T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3049 CG T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3050 CH T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3051 OI1 T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3052 C T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3053 N T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3054 H T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3055 H T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3056 CA T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3057 CB T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3058 CG T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3059 CH T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3060 OI1 T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3061 C T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3062 N T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3063 H T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3064 H T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3065 CA T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3066 CB T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3067 CG T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3068 CH T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3069 OI1 T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3070 C T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3071 N T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3072 H T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3073 H T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3074 CA T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3075 CB T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3076 CG T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3077 CH T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3078 OI1 T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3079 C T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3080 N T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3081 H T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3082 H T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3083 CA T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3084 CB T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3085 CG T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3086 CH T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3087 OI1 T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3088 C T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3089 N T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3090 H T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3091 H T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3092 CA T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3093 CB T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3094 CG T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3095 CH T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3096 OI1 T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3097 C T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3098 N T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3099 H T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3100 H T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3101 CA T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3102 CB T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3103 CG T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3104 CH T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3105 OI1 T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3106 C T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3107 N T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3108 H T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3109 H T1S 441	54.369	40.571	-11.569	1.00	4.569	C1
ATOM 3110 CA T1S 441	54.369	40.571	-11.569			

FIGURE 5

ATOM 3059	CDI	LEU	451	58.833	32.784	-8.653	1.005912	CI	ATOM 3110	C	IE	457	47.048	31.618	-5.472	1.006176	CI
ATOM 3060	CDI	LEU	451	58.869	34.511	-7.751	1.005827	CI	ATOM 3111	N	PRO	458	45.961	31.761	-6.706	1.008257	CI
ATOM 3061	C	LEU	451	54.745	32.700	-9.280	1.005596	CI	ATOM 3112	N	PRO	458	45.961	31.761	-6.706	1.008257	CI
ATOM 3062	N	GLY	452	53.713	31.735	-8.119	1.005174	CI	ATOM 3113	CD	PRO	458	45.959	31.253	-1.279	1.008121	CI
ATOM 3063	N	GLY	452	53.889	34.241	-10.191	1.005100	CI	ATOM 3114	CD	PRO	458	44.607	31.643	-5.264	1.008174	CI
ATOM 3064	CA	GLY	452	52.567	33.515	-8.710	1.006066	CI	ATOM 3115	CD	PRO	458	44.757	30.792	-1.157	1.008112	CI
ATOM 3065	C	GLY	452	51.947	31.137	-7.772	1.006364	CI	ATOM 3116	CD	PRO	458	44.757	30.792	-1.157	1.008112	CI
ATOM 3066	N	ILE	453	52.089	31.545	-9.969	1.006846	CI	ATOM 3117	C	PRO	458	44.120	31.053	-5.448	1.007930	CI
ATOM 3067	N	ILE	453	52.628	32.000	-10.618	1.006000	CI	ATOM 3118	Q	PRO	458	44.874	33.736	-4.718	1.008010	CI
ATOM 3068	CA	ILE	453	51.406	30.205	-10.326	1.007127	CI	ATOM 3119	H	PRO	458	44.814	33.185	-2.701	1.007819	CI
ATOM 3069	CG	ILE	453	51.421	31.061	-12.777	1.007181	CI	ATOM 3120	H	PRO	458	44.814	33.185	-2.701	1.007819	CI
ATOM 3070	CDI	ILE	453	50.599	32.148	-12.498	1.007929	CI	ATOM 3121	CA	TRP	459	43.534	34.986	-7.091	1.007173	CI
ATOM 3071	CDI	ILE	453	51.486	31.744	-14.012	1.007934	CI	ATOM 3122	CG	TRP	459	43.802	35.428	-8.222	1.007871	CI
ATOM 3072	NEI	ILE	453	50.613	32.923	-11.551	1.007985	CI	ATOM 3123	CG	TRP	459	43.802	35.428	-8.222	1.007871	CI
ATOM 3073	NEI	ILE	453	51.315	32.382	-14.470	1.008111	CI	ATOM 3124	CDI	TRP	459	41.802	36.771	-9.618	1.008129	CI
ATOM 3074	NEI	ILE	453	50.230	33.225	-11.586	1.007985	CI	ATOM 3125	CDI	TRP	459	40.718	35.960	-9.915	1.008428	CI
ATOM 3075	NEI	ILE	453	51.735	34.068	-14.581	1.008111	CI	ATOM 3126	CDI	TRP	459	40.718	35.960	-9.915	1.008428	CI
ATOM 3076	NEI	ILE	453	50.230	33.225	-11.586	1.007985	CI	ATOM 3127	CDI	TRP	459	42.818	38.763	-9.460	1.008523	CI
ATOM 3077	CG	ILE	453	51.735	34.068	-14.581	1.008111	CI	ATOM 3128	HEI	TRP	459	42.944	39.218	-9.483	1.008101	CI
ATOM 3078	CG	ILE	453	51.735	34.068	-14.581	1.008111	CI	ATOM 3129	HEI	TRP	459	42.944	39.218	-9.483	1.008101	CI
ATOM 3079	CG	ILE	453	51.735	34.068	-14.581	1.008111	CI	ATOM 3130	CGI	TRP	459	39.638	38.738	-10.494	1.008417	CI
ATOM 3080	N	SER	454	53.745	29.207	-9.651	1.007464	CI	ATOM 3131	CGI	TRP	459	39.562	37.904	-10.852	1.009483	CI
ATOM 3081	N	SER	454	54.714	29.739	-10.351	1.007464	CI	ATOM 3132	CGI	TRP	459	42.009	35.013	-6.217	1.007211	CI
ATOM 3082	CG	SER	454	51.149	27.711	-8.306	1.007000	CI	ATOM 3133	C	TRP	459	41.802	36.771	-9.618	1.008129	CI
ATOM 3083	CG	SER	454	56.123	28.762	-8.980	1.007134	CI	ATOM 3134	N	ALA	460	41.557	35.969	-6.400	1.007488	CI
ATOM 3084	CG	SER	454	57.092	27.715	-9.124	1.007528	CI	ATOM 3135	N	ALA	460	42.187	36.640	-5.889	1.007488	CI
ATOM 3085	CG	SER	454	54.710	27.617	-6.535	1.008037	CI	ATOM 3136	N	ALA	460	42.187	36.640	-5.889	1.007488	CI
ATOM 3086	N	SER	454	54.070	29.789	-6.693	1.007972	CI	ATOM 3137	CA	ALA	460	39.449	37.076	-6.534	1.007638	CI
ATOM 3087	N	SER	454	53.950	30.582	-7.150	1.008091	CI	ATOM 3138	CA	ALA	460	39.449	37.076	-6.534	1.007638	CI
ATOM 3088	N	SER	454	53.950	30.582	-7.150	1.008091	CI	ATOM 3139	CA	ALA	460	39.449	37.076	-6.534	1.007638	CI
ATOM 3089	N	SER	454	53.950	30.582	-7.150	1.008091	CI	ATOM 3140	O	ALA	460	39.449	37.076	-6.534	1.007638	CI
ATOM 3090	N	SER	454	53.950	30.582	-7.150	1.008091	CI	ATOM 3141	O	ALA	460	39.449	37.076	-6.534	1.007638	CI
ATOM 3091	CG	LEU	455	54.083	31.947	-4.838	1.008020	CI	ATOM 3142	CG	LEU	461	37.242	36.793	-8.868	1.007546	CI
ATOM 3092	CG	LEU	455	55.389	31.981	-5.269	1.008167	CI	ATOM 3143	CG	LEU	461	37.242	36.793	-8.868	1.007546	CI
ATOM 3093	CG	LEU	455	52.254	31.979	-5.419	1.008126	CI	ATOM 3144	CG	LEU	461	36.605	35.605	-8.755	1.007571	CI
ATOM 3094	CG	LEU	455	52.254	31.979	-5.419	1.008126	CI	ATOM 3145	CG	LEU	461	36.605	35.605	-8.755	1.007571	CI
ATOM 3095	CG	LEU	455	52.254	31.979	-5.419	1.008126	CI	ATOM 3146	CG	LEU	461	36.605	35.605	-8.755	1.007571	CI
ATOM 3096	CG	LEU	455	52.254	31.979	-5.419	1.008126	CI	ATOM 3147	O	PRO	461	35.677	37.734	-6.440	1.007346	CI
ATOM 3097	O	LEU	455	52.318	29.510	-4.448	1.008136	CI	ATOM 3148	N	LEU	462	35.996	38.767	-8.449	1.007719	CI
ATOM 3098	O	LEU	455	52.018	29.893	-3.741	1.008122	CI	ATOM 3149	N	LEU	462	35.996	38.767	-8.449	1.007719	CI
ATOM 3099	N	GLY	456	51.032	24.917	-5.194	1.006000	CI	ATOM 3150	CA	LEU	462	35.969	39.891	-8.725	1.007487	CI
ATOM 3100	N	GLY	456	50.269	28.361	-5.467	1.008122	CI	ATOM 3151	CG	LEU	462	35.674	40.984	-6.388	1.007849	CI
ATOM 3101	C	GLY	456	49.210	29.386	-4.973	1.008126	CI	ATOM 3152	CG	LEU	462	34.786	41.959	-6.758	1.007849	CI
ATOM 3102	Q	GLY	456	49.442	30.697	-4.386	1.008124	CI	ATOM 3153	CG	LEU	462	34.786	41.959	-6.758	1.007849	CI
ATOM 3103	Q	GLY	456	49.442	30.697	-4.386	1.008124	CI	ATOM 3154	CG	LEU	462	34.786	41.959	-6.758	1.007849	CI
ATOM 3104	N	ILE	457	50.075	30.942	-5.894	1.006000	CI	ATOM 3155	C	LEU	462	34.701	40.365	-6.811	1.008611	CI
ATOM 3105	CA	ILE	457	48.435	31.761	-4.824	1.008163	CI	ATOM 3156	C	LEU	462	34.701	40.365	-6.811	1.008611	CI
ATOM 3106	CG	ILE	457	48.435	31.761	-4.824	1.008163	CI	ATOM 3157	CG	LEU	462	33.606	40.847	-10.847	1.008124	CI
ATOM 3107	CGI	ILE	457	48.435	31.761	-4.824	1.008163	CI	ATOM 3158	CG	LEU	472	22.074	42.654	-4.426	1.008124	CI
ATOM 3108	CGI	ILE	457	48.435	31.761	-4.824	1.008163	CI	ATOM 3159	CG	LEU	472	22.074	42.654	-4.426	1.008124	CI
ATOM 3109	CGI	ILE	457	48.435	31.761	-4.824	1.008163	CI	ATOM 3160	CGI	LEU	472	22.074	42.654	-4.426	1.008124	CI

ATOM	3161	CG	LEU	472	23.501	44.883	-1.986	100.00	60.1535
ATOM	3162	C	LEU	472	23.504	40.225	-1.996	100.00	60.1391
ATOM	3163	O	LEU	472	23.338	39.874	-2.949	100.00	64.90
ATOM	3164	CG	LEU	472	23.503	44.883	-1.986	100.00	60.1535
ATOM	3165	H	LEU	472	21.563	41.441	-3.595	100.00	60.00
ATOM	3166	N	LEU	472	22.358	42.449	-1.160	100.00	60.00
ATOM	3167	H	LEU	472	22.358	42.449	-1.160	100.00	60.00
ATOM	3168	C	LEU	472	23.092	42.037	-0.733	100.00	63.85
ATOM	3169	H	LEU	472	23.092	42.037	-0.733	100.00	63.85
ATOM	3170	N	ALA	473	24.023	38.881	-0.518	100.00	60.00
ATOM	3171	C	ALA	473	24.023	38.881	-0.518	100.00	60.00
ATOM	3172	C	ALA	473	24.023	37.939	-0.538	100.00	63.65
ATOM	3173	C	ALA	473	25.196	38.354	-1.126	100.00	62.01
ATOM	3174	H	ALA	473	25.196	38.354	-1.126	100.00	62.01
ATOM	3175	O	ALA	473	26.381	40.511	-0.716	100.00	63.36
ATOM	3176	H	ALA	473	24.448	41.718	-2.274	100.00	60.00
ATOM	3177	C	GLY	474	24.161	37.137	-0.267	100.00	63.80
ATOM	3178	C	GLY	474	27.354	37.950	-3.316	100.00	65.13
ATOM	3179	H	GLY	474	27.354	37.950	-3.316	100.00	65.13
ATOM	3180	O	GLY	474	28.539	40.127	-0.885	100.00	64.74
ATOM	3181	H	GLY	474	26.401	39.510	-1.815	100.00	60.00
ATOM	3182	C	GLY	474	28.208	40.127	-0.885	100.00	64.74
ATOM	3183	C	GLY	475	27.935	41.1	-4.806	100.00	63.74
ATOM	3184	H	GLY	475	27.935	41.1	-4.806	100.00	63.74
ATOM	3185	C	GLY	475	28.995	40.767	-2.991	100.00	57.30
ATOM	3186	O	GLY	475	30.214	40.949	-2.724	100.00	57.14
ATOM	3187	N	LEU	476	32.310	40.983	-1.279	100.00	53.29
ATOM	3188	C	LEU	476	32.310	40.983	-1.279	100.00	53.29
ATOM	3189	H	LEU	476	32.310	40.983	-1.279	100.00	53.29
ATOM	3190	C	LEU	476	28.797	35.151	-4.953	100.00	60.00
ATOM	3191	CG	LEU	476	27.119	37.123	0.523	100.00	45.68
ATOM	3192	H	LEU	476	27.119	37.123	0.523	100.00	45.68
ATOM	3193	CG	LEU	476	27.130	43.159	0.497	100.00	42.80
ATOM	3194	C	LEU	476	26.670	43.159	0.497	100.00	36.35
ATOM	3195	C	LEU	476	26.670	43.159	0.497	100.00	36.35
ATOM	3196	N	SER	477	29.053	38.972	-0.270	100.00	50.67
ATOM	3197	H	SER	477	29.053	38.972	-0.270	100.00	50.67
ATOM	3198	C	SER	477	29.731	37.712	0.110	100.00	51.41
ATOM	3199	C	SER	477	29.731	37.712	0.110	100.00	51.41
ATOM	3200	CG	SER	477	27.732	36.616	-0.051	100.00	57.65
ATOM	3201	H	SER	477	27.732	36.616	-0.051	100.00	57.65
ATOM	3202	C	SER	477	30.382	37.543	-0.044	100.00	45.35
ATOM	3203	O	SER	477	31.980	37.543	-0.044	100.00	31.41
ATOM	3204	N	GLN	478	31.037	37.788	-1.994	100.00	50.21

ATOM	3312	HE2	GIN	478	29.645	36.921	2.537	1.00	0.00	C2
ATOM	3313	HE2	GIN	479	29.645	36.921	2.537	1.00	0.00	C2
ATOM	3314	C	GIN	478	31.398	38.670	2.249	1.00	0.00	C2
ATOM	3315	C	GIN	479	31.398	38.670	2.249	1.00	0.00	C2
ATOM	3316	C	GIN	478	31.454	38.713	2.197	1.00	0.01	C2
ATOM	3317	C	GIN	479	31.454	38.713	2.197	1.00	0.01	C2
ATOM	3318	C	LEU	479	32.131	40.223	1.859	1.00	0.478	C2
ATOM	3319	C	LEU	478	32.131	40.223	1.859	1.00	0.478	C2
ATOM	3320	C	LEU	479	34.015	40.146	1.555	1.00	0.573	C2
ATOM	3321	C	LEU	478	34.015	40.146	1.555	1.00	0.573	C2
ATOM	3322	C	LEU	479	35.434	42.141	0.467	1.00	0.475	C2
ATOM	3323	C	LEU	478	35.434	42.141	0.467	1.00	0.475	C2
ATOM	3324	C	LEU	479	32.596	42.033	1.118	1.00	0.478	C2
ATOM	3325	C	LEU	478	32.596	42.033	1.118	1.00	0.478	C2
ATOM	3326	C	LEU	479	33.759	43.258	2.230	1.00	0.482	C2
ATOM	3327	C	LEU	478	33.759	43.258	2.230	1.00	0.482	C2
ATOM	3328	C	LEU	479	34.504	40.146	0.036	1.00	0.473	C2
ATOM	3329	C	LEU	478	34.504	40.146	0.036	1.00	0.473	C2
ATOM	3330	C	HE2	480	31.669	39.750	0.763	1.00	0.00	C2
ATOM	3331	C	HE2	479	31.669	39.750	0.763	1.00	0.00	C2
ATOM	3332	C	HE2	480	32.658	39.829	0.763	1.00	0.00	C2
ATOM	3333	C	HE2	479	32.658	39.829	0.763	1.00	0.00	C2
ATOM	3334	C	HE2	480	33.094	38.241	4.369	1.00	0.481	C2
ATOM	3335	C	HE2	479	33.094	38.241	4.369	1.00	0.481	C2
ATOM	3336	C	HE2	480	31.123	38.593	4.709	1.00	0.454	C2
ATOM	3337	C	HE2	479	31.123	38.593	4.709	1.00	0.454	C2
ATOM	3338	C	HE2	480	31.263	38.593	4.544	1.00	0.427	C2
ATOM	3339	C	HE2	479	31.263	38.593	4.544	1.00	0.427	C2
ATOM	3340	C	HE2	480	31.500	36.986	5.965	1.00	0.314	C2
ATOM	3341	C	HE2	479	31.500	36.986	5.965	1.00	0.314	C2
ATOM	3342	C	HE2	480	32.760	38.241	4.644	1.00	0.00	C2
ATOM	3343	C	HE2	479	32.760	38.241	4.644	1.00	0.00	C2
ATOM	3344	C	HE2	480	35.716	37.631	7.791	1.00	0.403	C2
ATOM	3345	C	HE2	479	35.716	37.631	7.791	1.00	0.403	C2
ATOM	3346	C	HE2	480	34.615	37.029	0.015	1.00	0.924	C2
ATOM	3347	C	HE2	479	34.615	37.029	0.015	1.00	0.924	C2
ATOM	3348	C	HE2	480	35.391	35.818	0.061	1.00	0.837	C2
ATOM	3349	C	HE2	479	35.391	35.818	0.061	1.00	0.837	C2
ATOM	3350	C	HE2	480	34.413	34.943	0.100	1.00	0.404	C2
ATOM	3351	C	HE2	479	34.413	34.943	0.100	1.00	0.404	C2
ATOM	3352	C	HE2	480	34.595	35.927	-0.137	1.00	0.426	C2
ATOM	3353	C	HE2	479	34.595	35.927	-0.137	1.00	0.426	C2
ATOM	3354	C	HE2	480	36.724	36.272	0.111	1.00	0.612	C2
ATOM	3355	C	HE2	479	36.724	36.272	0.111	1.00	0.612	C2
ATOM	3356	C	HE2	480	33.958	37.790	0.765	1.00	0.243	C2
ATOM	3357	C	HE2	479	33.958	37.790	0.765	1.00	0.243	C2
ATOM	3358	C	HE2	480	35.928	37.490	1.168	1.00	0.050	C2
ATOM	3359	C	HE2	479	35.928	37.490	1.168	1.00	0.050	C2
ATOM	3360	C	HE2	480	38.020	37.792	1.866	1.00	0.350	C2
ATOM	3361	C	HE2	479	38.020	37.792	1.866	1.00	0.350	C2
ATOM	3362	C	HE2	480	38.358	38.296	0.151	1.00	0.614	C2
ATOM	3363	C	HE2	479	38.358	38.296	0.151	1.00	0.614	C2
ATOM	3364	C	HE2	480	38.381	38.040	0.750	1.00	0.464	C2
ATOM	3365	C	HE2	479	38.381	38.040	0.750	1.00	0.464	C2
ATOM	3366	C	HE2	480	37.455	39.426	0.608	1.00	0.000	C2
ATOM	3367	C	HE2	479	37.455	39.426	0.608	1.00	0.000	C2
ATOM	3368	C	HE2	480	36.375	41.687	1.081	1.00	0.511	C2
ATOM	3369	C	HE2	479	36.375	41.687	1.081	1.00	0.511	C2
ATOM	3370	C	HE2	480	38.650	38.441	0.136	1.00	0.304	C2
ATOM	3371	C	HE2	479	38.650	38.441	0.136	1.00	0.304	C2
ATOM	3372	C	HE2	480	40.332	38.908	3.749	1.00	0.315	C2
ATOM	3373	C	HE2	479	40.332	38.908	3.749	1.00	0.315	C2
ATOM	3374	C	HE2	480	41.500	37.263	7.265	1.00	0.408	C2
ATOM	3375	C	HE2	479	41.500	37.263	7.265	1.00	0.408	C2
ATOM	3376	C	HE2	480	41.905	36.478	3.783	1.00	0.404	C2
ATOM	3377	C	HE2	479	41.905	36.478	3.783	1.00	0.404	C2

FIGURE 5

ATOM 3263 C8 PHE 484	37975	31.300	3.015	1.003746	C2
ATOM 3264 C6 PHE 484	38119	32.884	4.482	1.004562	C2
ATOM 3265 C6 PHE 484	38328	34.445	6.710	1.004362	C2
ATOM 3266 C6 PHE 484	38421	34.858	5.795	1.004798	C2
ATOM 3267 C6 PHE 484	38427	35.179	6.710	1.004808	C2
ATOM 3268 C6 PHE 484	38677	35.603	6.710	1.003192	C2
ATOM 3270 C8 PHE 484	41162	35.289	3.816	1.003425	C2
ATOM 3271 N1 PHE 484	39577	35.717	1.250	1.000000	C2
ATOM 3273 N1 LEU 485	41475	34.278	1.163	1.003174	C2
ATOM 3274 CA LEU 485	41183	34.629	4.305	1.003515	C2
ATOM 3275 C6 LEU 485	41183	34.629	4.305	1.003515	C2
ATOM 3276 C6 LEU 485	41183	34.629	4.305	1.003515	C2
ATOM 3277 CD2 LEU 485	41183	34.629	4.305	1.003515	C2
ATOM 3278 CD2 LEU 485	41183	34.629	4.305	1.003515	C2
ATOM 3279 CD2 LEU 485	41183	34.629	4.305	1.003515	C2
ATOM 3280 N1 LEU 485	41183	34.629	4.305	1.003515	C2
ATOM 3281 N1 TYR 486	41609	36.815	1.034	1.003367	C2
ATOM 3282 H1 TYR 486	41757	37.186	0.659	1.000000	C2
ATOM 3283 C6 TYR 486	41757	37.186	0.659	1.000000	C2
ATOM 3284 C6 TYR 486	41757	37.186	0.659	1.000000	C2
ATOM 3285 CG TYR 486	41300	39.325	0.835	1.003337	C2
ATOM 3286 CD TYR 486	42134	38.405	1.579	1.003279	C2
ATOM 3287 CD TYR 486	42134	38.405	1.579	1.003279	C2
ATOM 3288 CD TYR 486	42134	38.405	1.579	1.003279	C2
ATOM 3289 CD TYR 486	42134	38.405	1.579	1.003279	C2
ATOM 3290 C2 TYR 486	44518	39.033	2.818	1.004463	C2
ATOM 3291 C2 TYR 486	44518	39.033	2.818	1.004463	C2
ATOM 3292 C2 TYR 486	44518	39.033	2.818	1.004463	C2
ATOM 3293 C2 TYR 486	44518	39.033	2.818	1.004463	C2
ATOM 3294 O TYR 486	44518	39.033	2.818	1.004463	C2
ATOM 3295 N1 LEU 485	44518	39.033	2.818	1.004463	C2
ATOM 3297 CA GLN 487	43135	37.646	0.031	1.002833	C2
ATOM 3298 CB GLN 487	43135	37.646	0.031	1.002833	C2
ATOM 3299 CG GLN 487	43135	37.646	0.031	1.002833	C2
ATOM 3300 CD GLN 487	43135	37.646	0.031	1.002833	C2
ATOM 3301 OE1 GLN 487	43135	37.646	0.031	1.002833	C2
ATOM 3302 NE2 GLN 487	43135	37.646	0.031	1.002833	C2
ATOM 3303 C1 GLN 487	43135	37.646	0.031	1.002833	C2
ATOM 3304 NE2 GLN 487	43135	37.646	0.031	1.002833	C2
ATOM 3305 C1 GLN 487	44791	36.455	5.007	1.002833	C2
ATOM 3306 O GLN 487	44791	36.455	5.007	1.002833	C2
ATOM 3307 N1 LEU 485	44791	36.455	5.007	1.002833	C2
ATOM 3308 N1 GLY 488	43799	35.400	3.824	1.000000	C2
ATOM 3309 CA GLY 488	43799	35.400	3.824	1.000000	C2
ATOM 3310 C1 GLY 488	43799	35.400	3.824	1.000000	C2
ATOM 3311 C1 GLY 488	43799	35.400	3.824	1.000000	C2
ATOM 3312 H1 LEU 485	46655	34.798	2.818	1.002503	C2
ATOM 3313 H1 LEU 485	45798	35.062	2.416	1.000000	C2
ATOM 3314 CA LEU 489	47931	34.970	2.099	1.002563	C2
ATOM 3315 C6 LEU 489	47931	34.970	2.099	1.002563	C2
ATOM 3316 C6 LEU 489	47931	34.970	2.099	1.002563	C2
ATOM 3317 CD LEU 489	47931	34.970	2.099	1.002563	C2
ATOM 3318 CD LEU 489	47931	34.970	2.099	1.002563	C2
ATOM 3319 C LEU 489	47931	34.970	2.099	1.002563	C2
ATOM 3320 C LEU 489	47931	34.970	2.099	1.002563	C2
ATOM 3321 C LEU 489	47931	34.970	2.099	1.002563	C2
ATOM 3322 H1 LEU 489	47931	34.970	2.099	1.002563	C2
ATOM 3323 CA LEU 489	47931	34.970	2.099	1.002563	C2
ATOM 3324 CA LEU 489	47931	34.970	2.099	1.002563	C2
ATOM 3325 CG LEU 489	47931	34.970	2.099	1.002563	C2
ATOM 3326 CH1 LEU 489	47931	34.970	2.099	1.002563	C2
ATOM 3327 CH1 LEU 489	47931	34.970	2.099	1.002563	C2
ATOM 3328 C LEU 489	47931	34.970	2.099	1.002563	C2
ATOM 3329 O LEU 489	47931	34.970	2.099	1.002563	C2
ATOM 3330 N1 GLN 491	48483	36.270	6.111	1.002588	C2
ATOM 3331 C1 GLN 491	48483	36.270	6.111	1.002588	C2
ATOM 3332 CA GLN 491	48483	36.270	6.111	1.002588	C2
ATOM 3333 C6 GLN 491	48483	36.270	6.111	1.002588	C2
ATOM 3334 C6 GLN 491	48483	36.270	6.111	1.002588	C2
ATOM 3335 C6 GLN 491	48483	36.270	6.111	1.002588	C2
ATOM 3336 OE1 GLN 491	48483	36.270	6.111	1.002588	C2
ATOM 3337 NE2 GLN 491	48483	36.270	6.111	1.002588	C2
ATOM 3338 NE2 GLN 491	48483	36.270	6.111	1.002588	C2
ATOM 3339 C1 GLN 491	48483	36.270	6.111	1.002588	C2
ATOM 3340 C1 GLN 491	48483	36.270	6.111	1.002588	C2
ATOM 3341 O GLN 491	48483	36.270	6.111	1.002588	C2
ATOM 3342 N1 ALA 492	50482	34.031	5.224	1.003415	C2
ATOM 3343 CA ALA 492	50482	34.031	5.224	1.003415	C2
ATOM 3344 CA ALA 492	50482	34.031	5.224	1.003415	C2
ATOM 3345 C6 ALA 492	50482	34.031	5.224	1.003415	C2
ATOM 3346 C6 ALA 492	50482	34.031	5.224	1.003415	C2
ATOM 3347 O ALA 492	50482	34.031	5.224	1.003415	C2
ATOM 3348 N1 LEU 489	50482	34.031	5.224	1.003415	C2
ATOM 3349 H1 LEU 489	50482	34.031	5.224	1.003415	C2
ATOM 3350 C1 LEU 489	50482	34.031	5.224	1.003415	C2
ATOM 3351 C1 LEU 489	50482	34.031	5.224	1.003415	C2
ATOM 3352 CG LEU 489	50482	34.031	5.224	1.003415	C2
ATOM 3353 CH1 LEU 489	50482	34.031	5.224	1.003415	C2
ATOM 3354 CH1 LEU 489	50482	34.031	5.224	1.003415	C2
ATOM 3355 C1 LEU 489	50482	34.031	5.224	1.003415	C2
ATOM 3356 O LEU 489	50482	34.031	5.224	1.003415	C2
ATOM 3357 N1 GLU 494	53395	36.900	3.749	1.003136	C2
ATOM 3358 CA GLU 494	53395	36.900	3.749	1.003136	C2
ATOM 3359 CA GLU 494	53395	36.900	3.749	1.003136	C2
ATOM 3360 C6 GLU 494	53395	36.900	3.749	1.003136	C2
ATOM 3361 C6 GLU 494	53395	36.900	3.749	1.003136	C2
ATOM 3362 C6 GLU 494	53395	36.900	3.749	1.003136	C2
ATOM 3363 OE1 GLU 494	53395	36.900	3.749	1.003136	C2
ATOM 3364 OE1 GLU 494	53395	36.900	3.749	1.003136	C2

FIGURES

ATOM 3365 C	GLU 494	55.865	36.835	8.343	1.00	44.31	C2
ATOM 3366 O	GLU 494	57.055	36.678	8.810	1.00	46.91	C2
ATOM 3367 N	GLY 495	55.338	38.046	8.114	1.00	44.32	C2
ATOM 3368 C	GLY 495	54.450	36.112	7.753	1.00	0.00	C2
ATOM 3369 O	GLY 495	57.035	36.965	7.238	1.00	37.36	C2
ATOM 3370 C	GLY 495	57.035	36.965	7.238	1.00	42.42	C2
ATOM 3371 N	ILE 496	57.310	38.802	6.279	1.00	41.04	C2
ATOM 3372 N	ILE 496	56.917	37.906	6.374	1.00	0.00	C2
ATOM 3373 C	ILE 496	57.929	40.210	4.753	1.00	38.60	C2
ATOM 3374 C	ILE 496	59.077	40.437	3.748	1.00	37.62	C2
ATOM 3375 CG1	ILE 496	56.662	39.964	3.440	1.00	36.39	C2
ATOM 3377 CG1	ILE 496	57.174	41.701	2.700	1.00	35.37	C2
ATOM 3378 N	ILE 496	57.035	36.965	7.238	1.00	42.42	C2
ATOM 3379 C	ILE 496	60.341	38.396	5.448	1.00	44.12	C2
ATOM 3380 O	ILE 496	59.998	40.228	6.533	1.00	44.31	C2
ATOM 3381 N	SER 497	62.331	41.964	3.170	1.00	40.74	C2
ATOM 3382 C	SER 497	62.046	40.727	2.897	1.00	0.00	C2
ATOM 3383 CG	SER 497	62.046	40.727	2.897	1.00	44.13	C2
ATOM 3384 C	SER 497	62.046	40.727	2.897	1.00	44.13	C2
ATOM 3385 CG	SER 497	62.046	40.727	2.897	1.00	44.13	C2
ATOM 3386 CG	SER 497	62.046	40.727	2.897	1.00	44.13	C2
ATOM 3387 N	SER 497	62.046	40.727	2.897	1.00	44.13	C2
ATOM 3388 O	SER 497	62.046	40.727	2.897	1.00	44.13	C2
ATOM 3389 N	PRO 498	62.164	41.490	9.971	1.00	44.96	C2
ATOM 3390 C	PRO 498	63.318	40.621	9.726	1.00	47.13	C2
ATOM 3391 O	PRO 498	63.318	40.621	9.726	1.00	47.13	C2
ATOM 3392 C	PRO 498	63.318	40.621	9.726	1.00	47.13	C2
ATOM 3393 C	PRO 498	63.318	40.621	9.726	1.00	47.13	C2
ATOM 3394 C	PRO 498	63.318	40.621	9.726	1.00	47.13	C2
ATOM 3395 N	GLU 499	61.760	43.799	9.983	1.00	45.27	C2
ATOM 3396 N	GLU 499	61.760	43.799	9.983	1.00	45.27	C2
ATOM 3397 N	GLU 499	61.760	43.799	9.983	1.00	45.27	C2
ATOM 3398 CA	GLU 499	61.731	43.699	8.391	1.00	48.06	C2
ATOM 3399 CA	GLU 499	61.731	43.699	8.391	1.00	48.06	C2
ATOM 3400 CG	GLU 499	64.001	46.187	7.100	1.00	37.51	C2
ATOM 3401 CG	GLU 499	64.544	44.737	7.076	1.00	60.61	C2
ATOM 3402 OEG	GLU 499	64.755	44.231	8.163	1.00	62.96	C2
ATOM 3403 OEG	GLU 499	64.755	44.231	8.163	1.00	62.96	C2
ATOM 3404 OEG	GLU 499	64.755	44.231	8.163	1.00	62.96	C2
ATOM 3405 O	GLU 499	60.349	40.895	9.981	1.00	46.54	C2
ATOM 3406 N	LEU 500	59.806	44.934	7.193	1.00	44.38	C2
ATOM 3407 N	LEU 500	59.806	44.934	7.193	1.00	44.38	C2
ATOM 3408 C	LEU 500	58.319	44.197	5.545	1.00	41.08	C2
ATOM 3409 CG	LEU 500	59.303	44.862	4.353	1.00	41.37	C2
ATOM 3410 CG	LEU 500	59.303	44.862	4.353	1.00	41.37	C2
ATOM 3411 CG1	LEU 500	59.716	43.818	3.257	1.00	45.04	C2
ATOM 3412 CG1	LEU 500	59.716	43.818	3.257	1.00	45.04	C2
ATOM 3413 C	LEU 500	57.455	44.521	7.628	1.00	40.59	C2
ATOM 3414 O	LEU 500	56.274	44.835	7.463	1.00	40.69	C2
ATOM 3415 N	GLY 501	57.866	44.835	8.085	1.00	39.37	C2
ATOM 3416 N	GLY 501	58.808	43.579	8.730	1.00	0.00	C2
ATOM 3417 O	GLY 501	58.808	43.579	8.730	1.00	0.00	C2
ATOM 3418 C	GLY 501	55.861	44.014	9.777	1.00	39.59	C2
ATOM 3419 O	GLY 501	55.861	44.014	9.777	1.00	39.59	C2
ATOM 3420 N	PRO 502	55.986	45.463	10.335	1.00	39.90	C2
ATOM 3421 N	PRO 502	57.237	45.908	11.735	1.00	41.18	C2
ATOM 3422 C	PRO 502	55.986	45.463	10.335	1.00	39.90	C2
ATOM 3423 C	PRO 502	55.986	45.463	10.335	1.00	39.90	C2
ATOM 3424 CG	PRO 502	56.989	47.405	11.231	1.00	41.36	C2
ATOM 3425 C	PRO 502	54.158	46.849	9.817	1.00	37.54	C2
ATOM 3426 C	PRO 502	54.158	46.849	9.817	1.00	37.54	C2
ATOM 3427 N	THR 503	55.663	46.638	8.499	1.00	0.00	C2
ATOM 3428 N	THR 503	55.663	46.638	8.499	1.00	0.00	C2
ATOM 3429 CA	THR 503	53.940	47.283	7.462	1.00	35.09	C2
ATOM 3430 CA	THR 503	53.940	47.283	7.462	1.00	35.09	C2
ATOM 3431 CG1	THR 503	55.857	48.946	6.845	1.00	0.00	C2
ATOM 3432 CG2	THR 503	55.857	48.946	6.845	1.00	0.00	C2
ATOM 3433 CG3	THR 503	55.857	48.946	6.845	1.00	0.00	C2
ATOM 3434 N	THR 503	54.197	48.162	5.176	1.00	35.56	C2
ATOM 3435 O	THR 503	54.197	48.162	5.176	1.00	35.56	C2
ATOM 3436 N	LEU 504	53.218	44.996	7.800	1.00	34.02	C2
ATOM 3437 N	LEU 504	53.218	44.996	7.800	1.00	34.02	C2
ATOM 3438 C	LEU 504	53.127	45.750	7.032	1.00	44.70	C2
ATOM 3439 CG	LEU 504	53.127	45.750	7.032	1.00	44.70	C2
ATOM 3440 CG	LEU 504	53.127	45.750	7.032	1.00	44.70	C2
ATOM 3441 CG1	LEU 504	54.163	40.977	5.667	1.00	37.07	C2
ATOM 3442 CG2	LEU 504	54.163	40.977	5.667	1.00	37.07	C2
ATOM 3443 CG3	LEU 504	54.163	40.977	5.667	1.00	37.07	C2
ATOM 3444 O	LEU 504	50.141	43.562	8.078	1.00	30.40	C2
ATOM 3445 N	ASP 505	51.736	44.106	9.551	1.00	26.09	C2
ATOM 3446 N	ASP 505	50.798	44.106	10.643	1.00	27.88	C2
ATOM 3447 CA	ASP 505	51.446	44.145	11.976	1.00	29.86	C2
ATOM 3448 CA	ASP 505	51.446	44.145	11.976	1.00	29.86	C2
ATOM 3449 CG	ASP 505	52.500	43.317	11.239	1.00	34.64	C2
ATOM 3450 CG1	ASP 505	51.779	43.544	13.224	1.00	37.40	C2
ATOM 3451 CG2	ASP 505	51.779	43.544	13.224	1.00	37.40	C2
ATOM 3452 C	ASP 505	49.661	45.060	10.568	1.00	28.61	C2
ATOM 3453 O	ASP 505	48.566	44.739	11.039	1.00	30.30	C2
ATOM 3454 N	THR 506	50.823	46.931	9.804	1.00	0.00	C2
ATOM 3455 N	THR 506	50.823	46.931	9.804	1.00	0.00	C2
ATOM 3456 CA	THR 506	48.860	47.225	9.731	1.00	25.74	C2
ATOM 3457 CB	THR 506	49.597	48.556	9.316	1.00	26.14	C2
ATOM 3458 CG	THR 506	49.597	48.556	9.316	1.00	26.14	C2
ATOM 3459 HGI	THR 506	49.243	49.072	11.746	1.00	0.00	C2
ATOM 3460 CG2	THR 506	48.594	49.517	8.619	1.00	24.46	C2
ATOM 3461 C	THR 506	48.012	46.735	8.615	1.00	24.80	C2
ATOM 3462 N	THR 506	48.012	46.735	8.615	1.00	24.80	C2
ATOM 3463 N	THR 506	48.012	46.735	8.615	1.00	24.80	C2
ATOM 3464 N	LEU 507	49.527	46.073	7.453	1.00	22.53	C2
ATOM 3465 CA	LEU 507	47.682	45.710	6.454	1.00	22.85	C2
ATOM 3466 CB	LEU 507	46.574	45.408	5.796	1.00	27.51	C2

FIGURE 5

ATOM 3467 CG LEU 507	48.010	44.519	3.858	1.00	70.85	C2
ATOM 3468 CD1 LEU 507	46.771	45.055	3.455	1.00	74.13	C2
ATOM 3469 CD2 LEU 507	49.074	45.055	2.842	1.00	70.13	C2
ATOM 3470 CE LEU 507	46.440	44.540	6.840	1.00	74.09	C2
ATOM 3471 O LEU 507	47.151	43.618	7.661	1.00	74.01	C2
ATOM 3472 N GIN 508	47.151	43.618	7.661	1.00	74.01	C2
ATOM 3473 H GIN 508	46.218	42.655	8.214	1.00	73.71	C2
ATOM 3474 H GIN 508	46.218	42.655	8.214	1.00	73.71	C2
ATOM 3475 CG GIN 508	47.937	40.199	8.178	1.00	71.83	C2
ATOM 3476 CD GIN 508	48.842	40.090	9.054	1.00	73.40	C2
ATOM 3477 OEI GIN 508	50.031	40.346	9.161	1.00	73.32	C2
ATOM 3478 OEI GIN 508	47.371	39.090	9.748	1.00	73.30	C2
ATOM 3479 HEI GIN 508	48.131	39.090	9.748	1.00	73.30	C2
ATOM 3480 HEI GIN 508	48.131	39.090	9.748	1.00	73.30	C2
ATOM 3481 HE2 GIN 508	48.131	38.633	10.060	1.00	73.00	C2
ATOM 3482 C GIN 508	45.103	43.173	9.111	1.00	74.24	C2
ATOM 3483 O GIN 508	43.978	42.650	9.014	1.00	74.06	C2
ATOM 3484 H GIN 508	44.116	42.650	10.070	1.00	76.07	C2
ATOM 3485 H GIN 508	44.116	42.650	10.070	1.00	76.07	C2
ATOM 3486 CA LEU 509	44.971	44.640	10.977	1.00	75.71	C2
ATOM 3487 CB LEU 509	44.971	44.640	10.977	1.00	75.71	C2
ATOM 3488 CB LEU 509	44.971	44.640	10.977	1.00	75.71	C2
ATOM 3489 CD1 LEU 509	46.558	44.173	11.042	1.00	75.00	C2
ATOM 3490 CD2 LEU 509	46.558	44.173	11.042	1.00	75.00	C2
ATOM 3491 C LEU 509	43.465	45.471	10.130	1.00	75.17	C2
ATOM 3492 N LEU 509	42.179	45.471	10.408	1.00	73.72	C2
ATOM 3493 H ASP 510	43.999	46.277	8.510	1.00	0.00	C2
ATOM 3494 H ASP 510	44.865	46.277	8.510	1.00	0.00	C2
ATOM 3495 CA ASP 510	42.955	46.998	8.240	1.00	72.66	C2
ATOM 3496 CB ASP 510	44.521	46.998	8.240	1.00	72.66	C2
ATOM 3497 CG ASP 510	44.521	46.998	8.240	1.00	72.66	C2
ATOM 3498 CD1 ASP 510	45.178	49.621	7.477	1.00	74.28	C2
ATOM 3499 CD2 ASP 510	43.988	49.709	9.250	1.00	74.44	C2
ATOM 3500 O ASP 510	42.197	49.709	9.250	1.00	74.44	C2
ATOM 3501 N VAL 511	42.197	49.709	9.250	1.00	74.44	C2
ATOM 3502 H VAL 511	43.611	44.900	6.620	1.00	0.00	C2
ATOM 3503 H VAL 511	43.611	44.900	6.620	1.00	0.00	C2
ATOM 3504 CA VAL 511	42.197	49.709	9.250	1.00	74.44	C2
ATOM 3505 CB VAL 511	42.197	49.709	9.250	1.00	74.44	C2
ATOM 3506 CG1 VAL 511	41.954	41.756	4.792	1.00	70.43	C2
ATOM 3507 CG2 VAL 511	43.529	43.324	4.210	1.00	16.19	C2
ATOM 3508 O VAL 511	39.625	43.447	6.719	1.00	73.46	C2
ATOM 3509 O VAL 511	39.625	43.447	6.719	1.00	73.46	C2
ATOM 3510 H ALA 512	41.258	43.017	8.163	1.00	70.49	C2
ATOM 3511 H ALA 512	42.716	43.063	8.161	1.00	0.00	C2
ATOM 3512 H ALA 512	42.716	43.063	8.161	1.00	0.00	C2
ATOM 3513 CA ALA 512	41.103	41.974	10.344	1.00	73.89	C2
ATOM 3514 C ALA 512	39.250	43.205	9.510	1.00	12.89	C2
ATOM 3515 O ALA 512	38.101	42.668	9.874	1.00	74.61	C2
ATOM 3516 N ASP 511	40.300	44.888	9.391	1.00	0.00	C2
ATOM 3517 H ASP 511	40.300	44.888	9.391	1.00	0.00	C2
ATOM 3518 C ASP 511	38.374	45.471	9.947	1.00	25.37	C2
ATOM 3519 CG ASP 511	39.648	46.277	8.510	1.00	0.00	C2
ATOM 3520 CD ASP 511	40.371	47.644	12.058	1.00	34.10	C2
ATOM 3521 CN1 ASP 511	39.580	45.646	12.058	1.00	34.10	C2
ATOM 3522 O ASP 511	35.792	45.710	8.461	1.00	74.95	C2
ATOM 3523 H PHE 514	37.867	45.719	7.634	1.00	72.88	C2
ATOM 3524 O ASP 511	35.792	45.710	8.461	1.00	74.95	C2
ATOM 3525 N PHE 514	38.839	45.614	7.475	1.00	24.09	C2
ATOM 3526 H PHE 514	38.839	45.614	7.475	1.00	24.09	C2
ATOM 3527 H PHE 514	38.839	45.614	7.475	1.00	24.09	C2
ATOM 3528 CB PHE 514	36.956	46.470	4.072	1.00	13.18	C2
ATOM 3529 CG PHE 514	35.715	47.089	4.245	1.00	13.18	C2
ATOM 3530 CN1 PHE 514	37.440	46.197	2.804	1.00	13.27	C2
ATOM 3531 CN2 PHE 514	35.687	46.197	2.804	1.00	14.53	C2
ATOM 3532 O PHE 514	36.983	46.519	3.120	1.00	14.53	C2
ATOM 3533 CD PHE 514	36.983	46.519	3.120	1.00	14.53	C2
ATOM 3534 C PHE 514	36.076	44.703	6.450	1.00	70.23	C2
ATOM 3535 C PHE 514	36.076	44.703	6.450	1.00	70.23	C2
ATOM 3536 H PHE 514	36.698	44.450	6.350	1.00	79.00	C2
ATOM 3537 N ALA 515	37.581	43.450	6.639	1.00	9.00	C2
ATOM 3538 H ALA 515	37.581	43.450	6.639	1.00	9.00	C2
ATOM 3539 CA ALA 515	35.839	42.260	6.416	1.00	37.86	C2
ATOM 3540 CB ALA 515	35.839	42.260	6.416	1.00	37.86	C2
ATOM 3541 C ALA 515	34.000	42.009	7.531	1.00	37.86	C2
ATOM 3542 O ALA 515	33.676	41.609	7.311	1.00	37.63	C2
ATOM 3543 N THR 516	35.164	42.457	8.735	1.00	35.01	C2
ATOM 3544 H THR 516	34.231	42.566	9.821	1.00	35.18	C2
ATOM 3545 CA THR 516	35.016	43.018	10.988	1.00	35.40	C2
ATOM 3546 CB THR 516	35.016	43.018	10.988	1.00	35.40	C2
ATOM 3547 CG1 THR 516	35.685	41.818	11.336	1.00	42.65	C2
ATOM 3548 CG2 THR 516	35.685	41.818	11.336	1.00	42.65	C2
ATOM 3549 CD1 THR 516	34.262	43.672	12.097	1.00	45.56	C2
ATOM 3550 C THR 516	33.140	43.534	9.487	1.00	37.67	C2
ATOM 3551 O THR 516	32.005	43.534	9.487	1.00	40.37	C2
ATOM 3552 H THR 516	34.291	44.850	8.469	1.00	0.00	C2
ATOM 3553 H THR 516	34.291	44.850	8.469	1.00	0.00	C2
ATOM 3554 CA THR 517	32.359	45.641	8.512	1.00	36.92	C2
ATOM 3555 CB THR 517	32.359	45.641	8.512	1.00	36.92	C2
ATOM 3556 CG1 THR 517	31.832	47.419	9.103	1.00	43.42	C2
ATOM 3557 CG2 THR 517	31.832	47.419	9.103	1.00	43.42	C2
ATOM 3558 CD1 THR 517	32.232	47.916	7.253	1.00	36.90	C2
ATOM 3559 CD2 THR 517	32.232	47.916	7.253	1.00	36.90	C2
ATOM 3560 O THR 517	30.137	45.135	7.811	1.00	38.49	C2
ATOM 3561 N ILE 518	31.790	44.344	6.466	1.00	75.54	C2
ATOM 3562 H ILE 518	32.795	44.386	6.597	1.00	0.00	C2
ATOM 3563 H ILE 518	32.795	44.386	6.597	1.00	0.00	C2
ATOM 3564 CB ILE 518	31.699	42.912	4.449	1.00	11.81	C2
ATOM 3565 CG1 ILE 518	30.703	42.202	3.555	1.00	11.46	C2
ATOM 3566 CG2 ILE 518	32.823	43.842	3.999	1.00	12.91	C2
ATOM 3567 H ILE 518	30.703	42.202	3.555	1.00	11.81	C2
ATOM 3568 C ILE 518	30.177	42.591	6.317	1.00	18.45	C2

FIGURE 5

ATOM 3560 O GIN 522	28.938	41.545	6.705	1.00	31.93	C2
ATOM 3561 H TBP 519	31.042	42.765	1.179	1.00	38.64	C2
ATOM 3572 CA TBP 519	31.781	41.959	7.361	1.00	38.15	C2
ATOM 3573 CB TBP 519	30.114	40.784	7.945	1.00	38.15	C2
ATOM 3574 CG TBP 519	30.493	38.793	9.255	1.00	42.26	C2
ATOM 3575 CH TBP 519	29.880	37.718	10.473	1.00	41.70	C2
ATOM 3576 CE TBP 519	29.648	37.778	10.305	1.00	41.69	C2
ATOM 3577 CE3 TBP 519	29.648	39.382	11.629	1.00	41.26	C2
ATOM 3578 CH TBP 519	29.788	37.695	8.419	1.00	42.92	C2
ATOM 3579 ME1 TBP 519	29.788	36.793	9.115	1.00	44.19	C2
ATOM 3580 ME2 TBP 519	29.788	36.793	9.115	1.00	44.19	C2
ATOM 3581 CE2 TBP 519	28.753	36.673	13.360	1.00	41.91	C2
ATOM 3582 CH2 TBP 519	28.964	38.666	12.652	1.00	41.77	C2
ATOM 3583 CH2 TBP 519	28.522	37.375	12.515	1.00	41.07	C2
ATOM 3584 C TBP 519	27.017	41.368	8.815	1.00	39.33	C2
ATOM 3585 N TBP 519	27.017	41.368	8.815	1.00	39.33	C2
ATOM 3586 N GIN 520	29.264	42.717	9.630	1.00	41.86	C2
ATOM 3587 H GIN 520	30.180	42.717	9.700	1.00	40.00	C2
ATOM 3588 CA GIN 520	28.240	42.016	10.464	1.00	44.63	C2
ATOM 3589 CB GIN 520	28.240	42.016	10.464	1.00	44.63	C2
ATOM 3590 CG GIN 520	29.602	41.008	12.343	1.00	40.14	C2
ATOM 3591 CD GIN 520	29.910	45.009	13.743	1.00	44.78	C2
ATOM 3592 OE1 GIN 520	28.988	45.566	13.154	1.00	61.62	C2
ATOM 3593 OE2 GIN 520	28.988	45.566	13.154	1.00	61.62	C2
ATOM 3594 ME3 GIN 520	31.749	46.260	12.932	1.00	40.00	C2
ATOM 3595 ME2 GIN 520	31.195	44.966	12.932	1.00	40.00	C2
ATOM 3596 C GIN 520	27.141	43.577	9.623	1.00	46.78	C2
ATOM 3597 N GIN 521	27.141	43.577	9.623	1.00	46.78	C2
ATOM 3598 N GIN 521	27.362	44.845	8.442	1.00	49.99	C2
ATOM 3599 H GIN 521	28.277	44.857	8.092	1.00	40.00	C2
ATOM 3600 CA GIN 521	26.236	44.638	7.716	1.00	49.02	C2
ATOM 3601 CB GIN 521	25.280	41.272	6.671	1.00	48.00	C2
ATOM 3602 CG GIN 521	25.456	46.726	5.790	1.00	50.87	C2
ATOM 3603 CD GIN 521	24.616	47.278	6.534	1.00	51.82	C2
ATOM 3604 OE1 GIN 521	24.864	47.694	7.671	1.00	52.47	C2
ATOM 3605 OE2 GIN 521	24.864	47.694	7.671	1.00	52.47	C2
ATOM 3606 ME2 GIN 521	23.092	47.455	4.987	1.00	0.00	C2
ATOM 3607 ME3 GIN 521	23.044	48.474	6.390	1.00	0.00	C2
ATOM 3608 C GIN 521	25.454	43.446	7.155	1.00	50.15	C2
ATOM 3609 N GIN 522	25.454	43.446	7.155	1.00	50.15	C2
ATOM 3610 N MET 522	26.057	42.144	6.668	1.00	49.18	C2
ATOM 3611 H MET 522	27.038	42.191	6.688	1.00	40.00	C2
ATOM 3612 CA MET 522	25.280	41.272	6.671	1.00	48.00	C2
ATOM 3613 CB MET 522	25.280	41.272	6.671	1.00	48.00	C2
ATOM 3614 CG MET 522	26.942	40.663	4.412	1.00	44.32	C2
ATOM 3615 SD MET 522	27.855	39.453	3.416	1.00	48.35	C2
ATOM 3616 CE MET 522	28.795	38.447	4.565	1.00	42.80	C2
ATOM 3617 C MET 522	28.795	38.447	4.565	1.00	42.80	C2
ATOM 3618 H MET 522	28.380	40.714	7.038	1.00	50.60	C2
ATOM 3619 N GIN 523	24.848	40.722	8.596	1.00	51.91	C2
ATOM 3620 H GIN 523						C2
ATOM 3621 CA GIN 523	23.766	41.031	8.749	1.00	49.83	C2
ATOM 3622 CB GIN 523	24.027	40.313	8.749	1.00	49.83	C2
ATOM 3623 CE GIN 523	24.634	40.722	11.081	1.00	54.53	C2
ATOM 3624 CD GIN 523	25.732	39.515	11.081	1.00	57.05	C2
ATOM 3625 OE1 GIN 523	24.515	38.187	10.485	1.00	61.61	C2
ATOM 3626 OE2 GIN 523	24.515	38.187	10.485	1.00	61.61	C2
ATOM 3627 C GIN 523	25.919	37.773	9.872	1.00	53.19	C2
ATOM 3628 CH GIN 523	22.773	41.116	9.736	1.00	58.79	C2
ATOM 3629 ME1 GIN 523	22.773	41.116	9.736	1.00	58.79	C2
ATOM 3630 ME2 GIN 523	22.773	41.116	9.736	1.00	58.79	C2
ATOM 3631 CA AIA 524	23.834	42.798	10.024	1.00	60.00	C2
ATOM 3632 CB AIA 524	23.834	42.798	10.024	1.00	60.00	C2
ATOM 3633 C AIA 524	20.382	44.768	9.992	1.00	54.11	C2
ATOM 3634 CA AIA 524	19.655	42.824	9.706	1.00	60.56	C2
ATOM 3635 N AIA 525	20.382	44.768	9.992	1.00	54.11	C2
ATOM 3636 N AIA 525	19.655	42.824	9.706	1.00	60.56	C2
ATOM 3637 CA AIA 525	21.196	43.083	7.693	1.00	66.44	C2
ATOM 3638 CB AIA 525	21.196	43.083	7.693	1.00	66.44	C2
ATOM 3639 C AIA 525	21.117	43.044	8.288	1.00	62.58	C2
ATOM 3640 CA AIA 525	19.841	41.536	6.558	1.00	71.11	C2
ATOM 3641 CB AIA 525	19.841	41.536	6.558	1.00	71.11	C2
ATOM 3642 H GIN 526	19.116	40.946	5.651	1.00	71.65	C2
ATOM 3643 CA GIN 526	21.019	40.780	6.043	1.00	70.00	C2
ATOM 3644 CB GIN 526	21.019	40.780	6.043	1.00	70.00	C2
ATOM 3645 C GIN 526	20.150	38.805	7.842	1.00	76.20	C2
ATOM 3646 N MET 527	21.388	38.433	5.970	1.00	80.23	C2
ATOM 3647 H MET 527	21.759	39.337	5.075	1.00	0.00	C2
ATOM 3648 CA MET 527	22.355	39.337	5.075	1.00	81.73	C2
ATOM 3649 CB MET 527	22.355	39.337	5.075	1.00	81.73	C2
ATOM 3650 CG MET 527	22.385	39.719	3.740	1.00	83.57	C2
ATOM 3651 SD MET 527	23.364	40.523	2.446	1.00	87.64	C2
ATOM 3652 CE MET 527	23.364	40.523	2.446	1.00	87.64	C2
ATOM 3653 C MET 527	22.974	35.357	5.324	1.00	81.84	C2
ATOM 3654 OT1 MET 527	22.974	35.357	5.324	1.00	81.84	C2
ATOM 3655 OT2 MET 527	23.940	37.104	4.502	1.00	82.99	C2
ATOM 3656 OT3 MET 527	23.940	37.104	4.502	1.00	82.99	C2
ATOM 3657 CG MET 528	47.397	30.041	4.517	1.00	72.15	C2
ATOM 3658 SD MET 528	46.205	30.708	5.604	1.00	79.03	C2
ATOM 3659 CE MET 528	44.850	31.067	2.515	1.00	77.20	C2
ATOM 3660 C MET 528	49.130	36.745	0.405	1.00	77.11	C2
ATOM 3661 H MET 528	46.723	26.401	1.917	1.00	81.00	C2
ATOM 3662 BT1 MET 528	47.353	26.068	1.449	1.00	0.00	C2
ATOM 3663 BT2 MET 528	47.353	26.068	1.449	1.00	0.00	C2
ATOM 3664 H MET 528	46.723	26.401	1.917	1.00	81.00	C2
ATOM 3665 IIT MET 528	47.153	27.400	0.795	1.00	76.57	C2
ATOM 3666 CA MET 528	47.153	27.400	0.795	1.00	76.57	C2
ATOM 3667 N PNO 529	50.089	29.070	0.274	1.00	72.55	C2
ATOM 3668 CB PNO 529	50.536	29.070	0.274	1.00	72.55	C2
ATOM 3669 CA PNO 529	50.677	30.165	1.006	1.00	71.49	C2
ATOM 3670 CB PNO 529						C2

FIGURE 5

ATOM 3671	CG	PRO	539	49.437	30.503	-1.837	1.00	71.52	C3
ATOM 3672	C	PRO	539	52.720	28.931	0.991	1.00	67.83	C3
ATOM 3673	N	PRO	539	50.484	28.417	0.961	1.00	66.48	C3
ATOM 3674	C	ALA	540	52.858	28.098	0.111	1.00	0.00	C3
ATOM 3675	CA	ALA	540	53.389	28.498	2.112	1.00	61.83	C3
ATOM 3676	CB	ALA	540	54.000	28.931	1.996	1.00	57.37	C3
ATOM 3677	C	ALA	540	54.539	29.122	1.996	1.00	53.30	C3
ATOM 3678	O	ALA	540	54.539	29.016	0.301	1.00	51.30	C3
ATOM 3680	N	PIE	541	55.256	30.000	2.292	1.00	52.25	C3
ATOM 3681	CA	PIE	541	54.799	30.061	3.257	1.00	0.00	C3
ATOM 3682	CB	PIE	541	55.964	32.106	1.942	1.00	48.80	C3
ATOM 3684	CG	PIE	541	54.789	32.703	1.058	1.00	45.77	C3
ATOM 3685	CD	PIE	541	54.992	31.919	0.279	1.00	44.20	C3
ATOM 3686	CE	PIE	541	54.799	32.106	1.942	1.00	48.80	C3
ATOM 3687	CE1	PIE	541	51.901	33.207	1.074	1.00	43.98	C3
ATOM 3688	CE2	PIE	541	52.428	33.018	0.769	1.00	42.86	C3
ATOM 3689	CZ	PIE	541	52.623	33.147	-0.563	1.00	41.32	C3
ATOM 3690	C	PIE	541	52.623	33.147	-0.563	1.00	41.32	C3
ATOM 3691	O	PIE	541	58.000	30.061	3.257	1.00	45.35	C3
ATOM 3693	N	ALA	542	58.172	29.442	1.362	1.00	48.21	C3
ATOM 3694	CA	ALA	542	57.875	29.798	0.656	1.00	0.00	C3
ATOM 3695	CB	ALA	542	57.706	27.749	1.984	1.00	45.37	C3
ATOM 3696	C	ALA	542	55.706	27.749	1.984	1.00	45.37	C3
ATOM 3698	O	ALA	542	60.510	29.567	2.266	1.00	44.87	C3
ATOM 3699	N	SER	543	61.001	29.504	3.374	1.00	46.49	C3
ATOM 3700	CA	SER	543	61.016	31.038	1.908	1.00	40.31	C3
ATOM 3701	CB	SER	543	62.253	31.081	1.704	1.00	40.31	C3
ATOM 3702	CG	SER	543	62.391	31.481	-0.354	1.00	35.74	C3
ATOM 3703	CD	SER	543	62.391	31.481	-0.354	1.00	35.74	C3
ATOM 3704	C	SER	543	62.087	32.613	1.896	1.00	40.88	C3
ATOM 3705	O	SER	543	61.016	33.115	1.536	1.00	42.63	C3
ATOM 3706	N	ALA	544	63.170	33.883	2.310	1.00	31.84	C3
ATOM 3707	CA	ALA	544	63.170	33.883	2.310	1.00	31.84	C3
ATOM 3708	CB	ALA	544	64.035	34.816	2.345	1.00	31.73	C3
ATOM 3709	CG	ALA	544	64.340	35.450	2.408	1.00	35.74	C3
ATOM 3710	C	ALA	544	62.713	35.337	0.947	1.00	37.06	C3
ATOM 3711	N	PIE	545	63.157	34.481	-0.130	1.00	35.72	C3
ATOM 3712	CA	PIE	545	64.131	34.594	-0.010	1.00	0.00	C3
ATOM 3713	CB	PIE	545	65.992	35.268	-1.484	1.00	33.66	C3
ATOM 3714	CG	PIE	545	65.992	35.268	-1.484	1.00	33.66	C3
ATOM 3715	CD	PIE	545	64.340	34.742	-0.990	1.00	29.62	C3
ATOM 3716	C	PIE	545	62.317	33.788	-4.557	1.00	79.80	C3
ATOM 3717	CE1	PIE	545	63.371	35.915	-4.689	1.00	31.90	C3
ATOM 3718	CE2	PIE	545	63.371	35.915	-4.689	1.00	31.90	C3
ATOM 3719	CE3	PIE	545	62.717	36.113	-5.918	1.00	31.00	C3
ATOM 3721	CZ	PIE	545	61.955	35.150	-6.480	1.00	31.01	C3
ATOM 3722	C	PIE	545	61.955	35.150	-6.480	1.00	31.01	C3
ATOM 3723	O	PIE	545	60.901	33.660	-2.189	1.00	34.88	C3
ATOM 3724	N	GIN	546	60.912	33.847	-1.135	1.00	34.77	C3
ATOM 3725	CA	GIN	546	59.900	33.223	-0.558	1.00	0.00	C3
ATOM 3726	CB	GIN	546	59.900	33.223	-0.558	1.00	0.00	C3
ATOM 3727	CG	GIN	546	59.145	32.232	-1.140	1.00	34.85	C3
ATOM 3728	CG	GIN	546	59.582	31.585	-2.444	1.00	46.95	C3
ATOM 3729	CD	GIN	546	59.582	31.585	-2.444	1.00	46.95	C3
ATOM 3730	CE	GIN	546	59.374	30.085	-2.473	1.00	42.98	C3
ATOM 3731	CE2	GIN	546	59.374	30.085	-2.473	1.00	42.98	C3
ATOM 3732	CE3	GIN	546	59.339	29.442	-1.644	1.00	0.00	C3
ATOM 3733	CE4	GIN	546	59.476	29.944	-4.472	1.00	0.00	C3
ATOM 3734	CE5	GIN	546	59.154	28.481	-7.609	1.00	0.00	C3
ATOM 3735	O	GIN	546	57.429	34.850	-1.133	1.00	34.82	C3
ATOM 3736	N	ARG	547	58.907	34.919	0.465	1.00	11.09	C3
ATOM 3737	CA	ARG	547	59.750	34.566	0.811	1.00	0.00	C3
ATOM 3738	CB	ARG	547	58.907	34.919	0.465	1.00	11.09	C3
ATOM 3739	CG	ARG	547	58.813	35.874	2.601	1.00	31.74	C3
ATOM 3740	CG	ARG	547	57.906	35.224	3.623	1.00	37.02	C3
ATOM 3741	CD	ARG	547	58.444	33.858	4.076	1.00	40.56	C3
ATOM 3742	CE	ARG	547	58.444	33.858	4.076	1.00	40.56	C3
ATOM 3743	CE	ARG	547	60.389	33.924	3.620	1.00	0.00	C3
ATOM 3744	CZ	ARG	547	60.190	34.394	5.543	1.00	0.48	C3
ATOM 3745	CH1	ARG	547	59.361	34.532	6.593	1.00	51.97	C3
ATOM 3746	CH2	ARG	547	59.361	34.532	6.593	1.00	51.97	C3
ATOM 3747	CH3	ARG	547	59.731	34.763	7.493	1.00	0.00	C3
ATOM 3748	CH4	ARG	547	61.464	34.775	5.616	1.00	48.55	C3
ATOM 3749	CH5	ARG	547	62.015	34.409	4.768	1.00	0.00	C3
ATOM 3750	CH6	ARG	547	62.015	34.409	4.768	1.00	0.00	C3
ATOM 3751	C	ARG	547	58.167	37.181	0.590	1.00	32.76	C3
ATOM 3752	O	ARG	547	57.084	37.694	0.317	1.00	34.25	C3
ATOM 3753	N	ARG	548	59.348	37.717	0.205	1.00	31.54	C3
ATOM 3754	CA	ARG	548	59.348	37.717	0.205	1.00	31.54	C3
ATOM 3755	CB	ARG	548	60.995	39.213	0.949	1.00	25.47	C3
ATOM 3756	CB	ARG	548	60.995	39.213	0.949	1.00	25.47	C3
ATOM 3757	CG	ARG	548	61.820	39.361	0.794	1.00	26.11	C3
ATOM 3758	CG	ARG	548	61.820	39.361	0.794	1.00	26.11	C3
ATOM 3759	CH	ARG	548	64.644	39.164	1.089	1.00	32.40	C3
ATOM 3760	HE	ARG	548	63.572	38.843	1.975	1.00	0.00	C3
ATOM 3761	CZ	ARG	548	63.544	39.518	1.375	1.00	32.66	C3
ATOM 3762	CH1	ARG	548	61.007	40.170	0.610	1.00	0.00	C3
ATOM 3763	CH2	ARG	548	61.007	40.170	0.610	1.00	0.00	C3
ATOM 3764	CH3	ARG	548	65.812	39.081	-0.606	1.00	0.00	C3
ATOM 3765	CH4	ARG	548	65.812	39.081	-0.606	1.00	0.00	C3
ATOM 3766	CH5	ARG	548	65.327	39.518	2.549	1.00	22.03	C3
ATOM 3767	CH6	ARG	548	65.327	39.518	2.549	1.00	22.03	C3
ATOM 3768	C	ARG	548	65.250	39.275	3.321	1.00	0.00	C3
ATOM 3769	N	ARG	548	58.713	38.997	-1.832	1.00	29.83	C3
ATOM 3770	CA	ARG	548	58.713	38.997	-1.832	1.00	29.83	C3
ATOM 3771	CB	ARG	548	59.979	38.102	-2.761	1.00	27.87	C3
ATOM 3772	CB	ARG	548	59.979	38.102	-2.761	1.00	27.87	C3
ATOM 3773	CE	ARG	548	56.727	38.045	-3.984	1.00	27.18	C3

FIGURE 5

ATOM 3773 C	549	58.797	36.934	-4.857	1.00	18.72	C3
ATOM 3774 C	549	56.748	37.810	-3.770	1.00	15.91	C3
ATOM 3775 C	549	56.896	38.337	-4.468	1.00	16.03	C3
ATOM 3776 H	550	57.103	36.657	-2.185	1.00	1.00	C3
ATOM 3777 H	550	55.055	36.805	-2.457	1.00	16.08	C3
ATOM 3778 C	550	54.410	38.498	-2.075	1.00	16.94	C3
ATOM 3779 C	550	54.410	38.498	-2.075	1.00	16.94	C3
ATOM 3780 C	551	55.073	38.817	-0.934	1.00	16.59	C3
ATOM 3781 H	551	55.073	38.817	-0.934	1.00	16.59	C3
ATOM 3782 H	551	54.540	40.212	-0.779	1.00	16.51	C3
ATOM 3783 C	551	54.540	40.212	-0.779	1.00	16.51	C3
ATOM 3784 C	551	54.307	41.115	-1.994	1.00	16.47	C3
ATOM 3785 C	551	54.307	41.115	-1.994	1.00	16.47	C3
ATOM 3786 H	552	55.154	41.013	-2.012	1.00	15.81	C3
ATOM 3787 H	552	54.952	40.396	-2.934	1.00	1.00	C3
ATOM 3788 C	552	54.952	40.396	-2.934	1.00	1.00	C3
ATOM 3789 C	552	54.952	40.396	-2.934	1.00	1.00	C3
ATOM 3790 C	552	55.917	42.391	-0.941	1.00	16.53	C3
ATOM 3791 C	552	57.337	42.396	-4.594	1.00	16.44	C3
ATOM 3792 C	552	53.650	41.406	-4.820	1.00	16.05	C3
ATOM 3793 C	552	53.650	41.406	-4.820	1.00	16.05	C3
ATOM 3794 H	553	53.455	40.720	-3.748	1.00	1.00	C3
ATOM 3795 H	553	54.122	39.447	-4.908	1.00	1.00	C3
ATOM 3796 C	553	52.766	39.705	-5.915	1.00	12.80	C3
ATOM 3797 C	553	51.457	39.705	-5.915	1.00	14.86	C3
ATOM 3798 C	553	51.457	39.705	-5.915	1.00	14.86	C3
ATOM 3799 C	553	51.457	39.705	-5.915	1.00	14.86	C3
ATOM 3800 C	553	52.073	36.623	-7.093	1.00	14.41	C3
ATOM 3801 C	553	51.017	35.925	-5.114	1.00	12.72	C3
ATOM 3802 C	553	51.017	35.925	-5.114	1.00	12.72	C3
ATOM 3803 H	554	50.962	39.810	-3.803	1.00	14.37	C3
ATOM 3804 H	554	51.774	39.350	-3.195	1.00	1.00	C3
ATOM 3805 C	554	49.660	39.491	-3.195	1.00	16.36	C3
ATOM 3806 C	554	49.660	39.491	-3.195	1.00	16.36	C3
ATOM 3807 C	554	50.966	37.933	-4.818	1.00	13.95	C3
ATOM 3808 C	554	48.953	39.613	-0.482	1.00	15.58	C3
ATOM 3809 C	554	49.312	41.175	-2.960	1.00	17.53	C3
ATOM 3810 C	554	49.312	41.175	-2.960	1.00	17.53	C3
ATOM 3811 H	555	50.277	42.106	-2.716	1.00	16.04	C3
ATOM 3812 C	555	51.221	41.321	-2.658	1.00	1.00	C3
ATOM 3813 C	555	49.956	43.539	-7.509	1.00	18.57	C3
ATOM 3814 C	555	49.956	43.539	-7.509	1.00	18.57	C3
ATOM 3815 C	555	49.402	44.053	-3.403	1.00	16.12	C3
ATOM 3816 C	555	48.425	44.003	-3.847	1.00	16.01	C3
ATOM 3817 H	556	49.985	43.521	-4.319	1.00	16.46	C3
ATOM 3818 C	556	49.985	43.521	-4.319	1.00	16.46	C3
ATOM 3819 C	556	50.684	43.100	-4.312	1.00	16.09	C3
ATOM 3820 C	556	50.684	43.100	-4.312	1.00	16.09	C3
ATOM 3821 C	556	50.442	43.338	-8.344	1.00	17.48	C3
ATOM 3822 H	556	49.966	44.144	-6.374	1.00	1.00	C3
ATOM 3823 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3824 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3825 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3826 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3827 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3828 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3829 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3830 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3831 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3832 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3833 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3834 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3835 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3836 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3837 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3838 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3839 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3840 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3841 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3842 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3843 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3844 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3845 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3846 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3847 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3848 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3849 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3850 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3851 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3852 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3853 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3854 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3855 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3856 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3857 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3858 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3859 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3860 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3861 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3862 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3863 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3864 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3865 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3866 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3867 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3868 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3869 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3870 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3871 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3872 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3873 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3874 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3875 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3876 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3877 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3878 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3879 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3880 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3881 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3882 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3883 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3884 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3885 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3886 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3887 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3888 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3889 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3890 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3891 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3892 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3893 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3894 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3895 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3896 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3897 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3898 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3899 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3900 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3901 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3902 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3903 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3904 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3905 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3906 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3907 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3908 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3909 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3910 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3911 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3912 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3913 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3914 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3915 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3916 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3917 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3918 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3919 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3920 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3921 C	556	48.149	42.145	-6.454	1.00	13.78	C3
ATOM 3922 C	556	48.149	42.145	-6.454	1.00	13.	

FIGURE 5

ATOM 3875 C2 PHE 561	38.653	42.027	-2.631	1.0016	36.89	C3
ATOM 3876 C2 PHE 561	37.853	41.074	-3.008	1.0017	36.89	C3
ATOM 3877 C PHE 561	35.987	44.645	-5.505	1.0018	36.89	C3
ATOM 3878 O PHE 561	38.789	44.697	-5.731	1.0018	36.89	C3
ATOM 3879 N PHE 561	35.987	44.645	-5.505	1.0018	36.89	C3
ATOM 3880 N LBU 562	41.643	45.467	-4.707	1.0018	36.89	C3
ATOM 3881 CA LBU 562	40.033	46.617	-4.057	1.0018	36.89	C3
ATOM 3882 CB LBU 562	40.047	47.203	-3.074	1.0018	36.89	C3
ATOM 3883 CC LBU 562	41.047	46.411	-1.816	1.0018	36.89	C3
ATOM 3884 CD LBU 562	40.033	46.617	-4.057	1.0018	36.89	C3
ATOM 3885 CE LBU 562	39.794	46.551	-1.200	1.0018	36.89	C3
ATOM 3886 C LBU 562	39.586	47.669	-3.988	1.0018	36.89	C3
ATOM 3887 O LBU 562	35.880	48.104	-4.681	1.0018	36.89	C3
ATOM 3888 N LBU 562	40.033	46.617	-4.057	1.0018	36.89	C3
ATOM 3889 N LBU 562	40.033	46.617	-4.057	1.0018	36.89	C3
ATOM 3890 CA GLU 563	39.738	45.908	-5.966	1.0018	36.89	C3
ATOM 3891 CB GLU 563	40.660	45.142	-8.137	1.0018	36.89	C3
ATOM 3892 CC GLU 563	41.999	46.628	-7.687	1.0018	36.89	C3
ATOM 3893 CD GLU 563	42.101	46.713	-6.415	1.0018	36.89	C3
ATOM 3894 CE GLU 563	44.101	46.713	-6.415	1.0018	36.89	C3
ATOM 3895 OEB GLU 563	42.886	48.386	-9.108	1.0018	36.89	C3
ATOM 3896 C GLU 563	38.375	48.469	-7.466	1.0018	36.89	C3
ATOM 3897 O GLU 563	37.388	45.170	-7.270	1.0018	36.89	C3
ATOM 3898 N GLU 563	37.388	45.170	-7.270	1.0018	36.89	C3
ATOM 3899 II VAL 564	39.107	46.714	-8.074	1.0018	36.89	C3
ATOM 3900 CA VAL 564	37.057	46.683	-8.558	1.0018	36.89	C3
ATOM 3901 CB VAL 564	37.333	45.255	-9.041	1.0018	36.89	C3
ATOM 3902 CC VAL 564	38.281	45.348	-10.241	1.0018	36.89	C3
ATOM 3903 CD VAL 564	38.281	45.348	-10.241	1.0018	36.89	C3
ATOM 3904 C VAL 564	36.010	46.709	-7.442	1.0018	36.89	C3
ATOM 3905 O VAL 564	34.891	47.015	-7.697	1.0018	36.89	C3
ATOM 3906 N SER 565	37.313	46.171	-5.063	1.0018	36.89	C3
ATOM 3907 N SER 565	37.313	46.171	-5.063	1.0018	36.89	C3
ATOM 3908 CA SER 565	35.562	46.602	-5.064	1.0018	36.89	C3
ATOM 3909 CB SER 565	36.344	46.013	-3.894	1.0018	36.89	C3
ATOM 3910 CC SER 565	35.590	45.714	-2.731	1.0018	36.89	C3
ATOM 3911 CD SER 565	35.590	45.714	-2.731	1.0018	36.89	C3
ATOM 3912 C SER 565	33.167	47.063	-4.871	1.0018	36.89	C3
ATOM 3913 O SER 565	34.018	48.287	-4.446	1.0018	36.89	C3
ATOM 3914 N TTR 566	35.963	49.093	-5.114	1.0018	36.89	C3
ATOM 3915 CA TTR 566	35.318	50.474	-5.086	1.0018	36.89	C3
ATOM 3916 CB TTR 566	36.765	51.362	-5.164	1.0018	36.89	C3
ATOM 3917 CC TTR 566	36.715	51.672	-5.097	1.0018	36.89	C3
ATOM 3918 CD TTR 566	36.715	51.672	-5.097	1.0018	36.89	C3
ATOM 3919 C TTR 566	37.112	53.613	-1.151	1.0018	36.89	C3
ATOM 3920 CB TTR 566	36.109	53.797	-5.566	1.0018	36.89	C3
ATOM 3921 CC TTR 566	36.046	54.888	-5.441	1.0018	36.89	C3
ATOM 3922 CD TTR 566	36.046	54.888	-5.441	1.0018	36.89	C3
ATOM 3923 O TTR 566	36.046	54.888	-5.441	1.0018	36.89	C3
ATOM 3924 N TTR 566	36.046	54.888	-5.441	1.0018	36.89	C3
ATOM 3925 III TTR 566	36.046	54.888	-5.441	1.0018	36.89	C3
ATOM 3926 C TTR 566	34.524	50.696	-6.217	1.0018	36.89	C3
ATOM 3927 N ALA 567	35.176	51.776	-5.950	1.0018	36.89	C3
ATOM 3928 N ALA 567	35.176	51.776	-5.950	1.0018	36.89	C3
ATOM 3929 II ALA 567	35.176	51.776	-5.950	1.0018	36.89	C3
ATOM 3930 CA ALA 567	32.670	50.165	-8.490	1.0018	36.89	C3
ATOM 3931 CB ALA 567	32.670	50.165	-8.490	1.0018	36.89	C3
ATOM 3932 CC ALA 567	32.670	50.165	-8.490	1.0018	36.89	C3
ATOM 3933 CD ALA 567	32.670	50.165	-8.490	1.0018	36.89	C3
ATOM 3934 N VAL 568	31.226	50.008	-7.116	1.0018	36.89	C3
ATOM 3935 II VAL 568	31.226	50.008	-7.116	1.0018	36.89	C3
ATOM 3936 CA VAL 568	31.226	50.008	-7.116	1.0018	36.89	C3
ATOM 3937 CB VAL 568	31.226	50.008	-7.116	1.0018	36.89	C3
ATOM 3938 CC VAL 568	31.226	50.008	-7.116	1.0018	36.89	C3
ATOM 3939 CD VAL 568	31.226	50.008	-7.116	1.0018	36.89	C3
ATOM 3940 N VAL 568	31.226	50.008	-7.116	1.0018	36.89	C3
ATOM 3941 II VAL 568	31.226	50.008	-7.116	1.0018	36.89	C3
ATOM 3942 N LBU 569	31.075	48.737	-5.248	1.0018	36.89	C3
ATOM 3943 II LBU 569	31.075	48.737	-5.248	1.0018	36.89	C3
ATOM 3944 CA LBU 569	32.058	48.719	-5.243	1.0018	36.89	C3
ATOM 3945 CB LBU 569	32.058	48.719	-5.243	1.0018	36.89	C3
ATOM 3946 CC LBU 569	32.058	48.719	-5.243	1.0018	36.89	C3
ATOM 3947 CD LBU 569	32.058	48.719	-5.243	1.0018	36.89	C3
ATOM 3948 N LBU 569	32.058	48.719	-5.243	1.0018	36.89	C3
ATOM 3949 II LBU 569	32.058	48.719	-5.243	1.0018	36.89	C3
ATOM 3950 O LBU 569	32.058	48.719	-5.243	1.0018	36.89	C3
ATOM 3951 N ARG 570	30.180	51.391	-5.479	1.0018	36.89	C3
ATOM 3952 II ARG 570	30.180	51.391	-5.479	1.0018	36.89	C3
ATOM 3953 CA ARG 570	31.153	51.391	-5.479	1.0018	36.89	C3
ATOM 3954 CB ARG 570	30.390	51.391	-5.479	1.0018	36.89	C3
ATOM 3955 CC ARG 570	29.658	51.391	-5.479	1.0018	36.89	C3
ATOM 3956 CD ARG 570	29.658	51.391	-5.479	1.0018	36.89	C3
ATOM 3957 N ARG 570	29.658	51.391	-5.479	1.0018	36.89	C3
ATOM 3958 II ARG 570	29.658	51.391	-5.479	1.0018	36.89	C3
ATOM 3959 C ARG 570	29.051	56.991	-10.036	1.0018	36.89	C3
ATOM 3960 NII ARG 570	30.240	57.590	-10.036	1.0018	36.89	C3
ATOM 3961 CB ARG 570	30.240	57.590	-10.036	1.0018	36.89	C3
ATOM 3962 CC ARG 570	30.240	57.590	-10.036	1.0018	36.89	C3
ATOM 3963 CD ARG 570	30.240	57.590	-10.036	1.0018	36.89	C3
ATOM 3964 NII ARG 570	27.958	57.736	-10.134	1.0018	36.89	C3
ATOM 3965 CB ARG 570	27.958	57.736	-10.134	1.0018	36.89	C3
ATOM 3966 CC ARG 570	27.958	57.736	-10.134	1.0018	36.89	C3
ATOM 3967 O ARG 570	27.958	57.736	-10.134	1.0018	36.89	C3
ATOM 3968 N HIS 571	27.107	52.865	-6.709	1.0018	36.89	C3
ATOM 3969 II HIS 571	27.107	52.865	-6.709	1.0018	36.89	C3
ATOM 3970 CA HIS 571	27.107	52.865	-6.709	1.0018	36.89	C3
ATOM 3971 CB HIS 571	27.107	52.865	-6.709	1.0018	36.89	C3
ATOM 3972 CC HIS 571	27.107	52.865	-6.709	1.0018	36.89	C3
ATOM 3973 CD HIS 571	27.107	52.865	-6.709	1.0018	36.89	C3
ATOM 3974 NII HIS 571	27.107	52.865	-6.709	1.0018	36.89	C3
ATOM 3975 CB HIS 571	27.107	52.865	-6.709	1.0018	36.89	C3
ATOM 3976 CC HIS 571	27.107	52.865	-6.709	1.0018	36.89	C3
ATOM 3977 O HIS 571	27.107	52.865	-6.709	1.0018	36.89	C3

FIGURE 5

ATOM 3977 MEI H15 571	29.994	50.518	-12.187	1.00	66.28	C3
ATOM 3978 MEI H15 571	29.601	50.468	-13.119	1.00	66.28	C3
ATOM 3979 MEI H15 571	29.632	49.759	-11.955	1.00	66.28	C3
ATOM 3980 C H15 571	26.520	49.759	-11.955	1.00	66.28	C3
ATOM 3981 N H15 571	26.520	48.963	-6.158	1.00	81.31	C3
ATOM 3982 H LBU 572	27.474	48.247	-5.915	1.00	0.00	C3
ATOM 3983 C LBU 572	27.474	48.457	-5.241	1.00	81.71	C3
ATOM 3984 C LBU 572	27.474	48.457	-5.241	1.00	81.71	C3
ATOM 3985 CG LBU 572	25.439	45.884	-4.721	1.00	81.71	C3
ATOM 3986 CDB LBU 572	25.783	45.386	-4.127	1.00	84.16	C3
ATOM 3987 CDB LBU 572	25.958	44.866	-3.714	1.00	84.08	C3
ATOM 3988 C LBU 572	26.997	49.511	-4.261	1.00	84.78	C3
ATOM 3989 C LBU 572	26.997	49.511	-4.261	1.00	84.78	C3
ATOM 3990 N ALA 573	25.169	50.795	-9.638	1.00	0.00	C3
ATOM 3991 H ALA 573	26.020	50.980	-5.174	1.00	85.90	C3
ATOM 3992 CA ALA 573	24.822	51.923	-3.721	1.00	85.90	C3
ATOM 3993 C ALA 573	25.000	52.207	-3.970	1.00	85.79	C3
ATOM 3994 C ALA 573	25.169	50.795	-9.638	1.00	0.00	C3
ATOM 3995 OT1 ALA 573	22.610	52.413	-3.099	1.00	81.33	C3
ATOM 3996 OT2 ALA 573	26.735	24.280	-5.161	1.00	27.42	W
ATOM 3997 OH2 H2O 603	35.843	42.530	-6.958	1.00	18.90	W
ATOM 3998 OH2 H2O 603	35.843	42.530	-6.958	1.00	18.90	W
ATOM 3999 H2 H2O 603	36.248	23.335	-4.997	1.00	0.00	W
ATOM 4000 OH2 H2O 603	47.880	37.960	12.073	1.00	56.30	W
ATOM 4001 H1 H2O 605	47.748	37.874	13.031	1.00	0.00	W
ATOM 4002 H1 H2O 605	46.980	37.838	11.753	1.00	0.00	W
ATOM 4003 H1 H2O 605	46.980	37.838	11.753	1.00	0.00	W
ATOM 4004 H1 H2O 607	40.471	48.761	7.909	1.00	0.00	W
ATOM 4005 H2 H2O 607	40.123	48.642	6.937	1.00	0.00	W
ATOM 4006 OH2 H2O 610	55.843	42.530	-6.958	1.00	18.90	W
ATOM 4007 OH2 H2O 610	55.843	42.530	-6.958	1.00	18.90	W
ATOM 4008 H2 H2O 610	55.185	42.046	-10.160	1.00	0.00	W
ATOM 4009 OH2 H2O 611	57.178	35.940	-14.220	1.00	34.63	W
ATOM 4010 H1 H2O 611	57.178	35.945	-14.974	1.00	0.00	W
ATOM 4011 H1 H2O 611	57.178	35.945	-14.974	1.00	0.00	W
ATOM 4012 OH2 H2O 612	75.793	27.337	19.130	1.00	78.21	W
ATOM 4013 H1 H2O 612	26.709	27.661	19.145	1.00	0.00	W
ATOM 4014 H2 H2O 612	25.782	26.792	19.939	1.00	0.00	W
ATOM 4015 H1 H2O 615	79.113	34.592	10.308	1.00	0.00	W
ATOM 4016 H2 H2O 615	79.113	34.592	10.308	1.00	0.00	W
ATOM 4017 H2 H2O 615	79.113	34.592	10.308	1.00	0.00	W
ATOM 4018 OH2 H2O 617	37.316	40.013	10.872	1.00	35.21	W
ATOM 4019 H1 H2O 617	36.608	40.016	11.259	1.00	0.00	W
ATOM 4020 H1 H2O 617	36.608	40.016	11.259	1.00	0.00	W
ATOM 4021 OH2 H2O 619	40.637	52.774	-7.287	1.00	29.62	W
ATOM 4022 H1 H2O 619	40.637	52.774	-7.287	1.00	0.00	W
ATOM 4023 H2 H2O 619	39.505	52.774	-7.287	1.00	0.00	W
ATOM 4024 OH2 H2O 621	72.553	32.407	10.464	1.00	19.99	W
ATOM 4025 H1 H2O 621	27.553	32.407	11.141	1.00	0.00	W
ATOM 4026 H2 H2O 621	27.553	32.407	11.141	1.00	0.00	W
ATOM 4027 OH2 H2O 623	25.057	31.972	11.675	1.00	32.70	W
ATOM 4028 H1 H2O 632	24.893	31.417	14.215	1.00	0.00	W
ATOM 4029 H2 H2O 632	24.469	31.417	14.215	1.00	0.00	W
ATOM 4030 OH2 H2O 633	20.791	28.593	14.215	1.00	50.17	W
ATOM 4031 H1 H2O 633	20.499	28.403	13.375	1.00	0.00	W
ATOM 4032 H2 H2O 633	20.499	28.403	13.375	1.00	0.00	W
ATOM 4033 OH2 H2O 635	22.166	28.593	14.488	1.00	0.00	W
ATOM 4034 H1 H2O 635	21.938	28.593	14.488	1.00	0.00	W
ATOM 4035 H2 H2O 635	22.166	28.593	14.488	1.00	0.00	W
ATOM 4036 OH2 H2O 636	23.649	36.486	9.710	1.00	23.36	W
ATOM 4037 H1 H2O 636	23.649	36.486	9.710	1.00	0.00	W
ATOM 4038 H2 H2O 636	23.649	36.486	9.710	1.00	0.00	W
ATOM 4039 OH2 H2O 637	42.033	78.320	5.097	1.00	46.19	W
ATOM 4040 H1 H2O 637	42.416	77.450	5.832	1.00	0.00	W
ATOM 4041 H2 H2O 637	42.416	77.450	5.832	1.00	0.00	W
ATOM 4042 OH2 H2O 639	47.327	31.417	14.215	1.00	0.00	W
ATOM 4043 H1 H2O 639	47.533	32.209	5.899	1.00	0.00	W
ATOM 4044 H2 H2O 639	47.533	32.209	5.899	1.00	0.00	W
ATOM 4045 OH2 H2O 641	47.442	30.713	5.714	1.00	0.00	W
ATOM 4046 H1 H2O 641	47.442	30.713	5.714	1.00	0.00	W
ATOM 4047 H2 H2O 641	47.442	30.713	5.714	1.00	0.00	W
ATOM 4048 OH2 H2O 643	24.469	36.486	9.710	1.00	23.36	W
ATOM 4049 H1 H2O 643	24.469	36.486	9.710	1.00	0.00	W
ATOM 4050 H2 H2O 643	24.469	36.486	9.710	1.00	0.00	W
ATOM 4051 OH2 H2O 645	28.192	67.028	6.876	1.00	0.00	W
ATOM 4052 H1 H2O 645	28.192	67.028	6.876	1.00	0.00	W
ATOM 4053 H2 H2O 645	28.192	67.028	6.876	1.00	0.00	W
ATOM 4054 OH2 H2O 647	51.535	67.904	0.814	1.00	0.00	W
ATOM 4055 H1 H2O 647	51.535	67.904	0.814	1.00	0.00	W
ATOM 4056 H2 H2O 647	51.535	67.904	0.814	1.00	0.00	W
ATOM 4057 OH2 H2O 649	62.897	38.367	3.759	1.00	73.55	W
ATOM 4058 H1 H2O 649	62.897	38.367	3.759	1.00	0.00	W
ATOM 4059 H2 H2O 649	62.897	38.367	3.759	1.00	0.00	W
ATOM 4060 OH2 H2O 651	29.587	68.480	-9.555	1.00	0.00	W
ATOM 4061 H1 H2O 651	29.587	68.480	-9.555	1.00	0.00	W
ATOM 4062 H2 H2O 651	29.587	68.480	-9.555	1.00	0.00	W
ATOM 4063 OH2 H2O 653	51.408	56.331	4.056	1.00	62.90	W
ATOM 4064 H1 H2O 653	50.718	56.331	3.365	1.00	0.00	W
ATOM 4065 H2 H2O 653	50.718	56.331	3.365	1.00	0.00	W
ATOM 4066 OH2 H2O 655	49.442	55.351	1.474	1.00	0.00	W
ATOM 4067 H1 H2O 655	49.442	55.351	1.474	1.00	0.00	W
ATOM 4068 H2 H2O 655	49.442	55.351	1.474	1.00	0.00	W
ATOM 4069 OH2 H2O 657	68.715	42.794	-23.563	1.00	40.77	W
ATOM 4070 H1 H2O 657	68.715	42.794	-23.563	1.00	0.00	W
ATOM 4071 H2 H2O 657	68.715	42.794	-23.563	1.00	0.00	W
ATOM 4072 OH2 H2O 659	66.374	40.425	-2.469	1.00	47.31	W
ATOM 4073 H1 H2O 659	66.374	40.425	-2.469	1.00	0.00	W
ATOM 4074 H2 H2O 659	66.374	40.425	-2.469	1.00	0.00	W
ATOM 4075 OH2 H2O 661	66.307	42.017	-4.993	1.00	44.08	W
ATOM 4076 H1 H2O 661	66.307	42.017	-4.993	1.00	0.00	W
ATOM 4077 H2 H2O 661	66.307	42.017	-4.993	1.00	0.00	W
ATOM 4078 OH2 H2O 663	46.321	31.417	14.215	1.00	0.00	W

FIGURE 5

ATOM	4079	H1	H2O	657	39.958	56.259	5.613	1.00	0.00	W
ATOM	4080	H2	H2O	657	-40.021	57.651	-5.014	1.00	0.00	W
ATOM	4081	OH2	H2O	658	48.780	47.580	-3.172	1.00	51.09	W
ATOM	4082	H1	H2O	658	48.811	46.671	-3.438	1.00	0.00	W
ATOM	4083	H2	H2O	658	49.568	47.955	-3.542	1.00	0.00	W
ATOM	4084	OH2	H2O	663	29.055	62.889	1.823	1.00	39.23	W
ATOM	4085	H1	H2O	663	29.380	62.827	2.739	1.00	0.00	W
ATOM	4086	H2	H2O	663	28.377	63.526	1.887	1.00	0.00	W
ATOM	4087	OH2	H2O	664	27.132	25.640	7.950	1.00	50.65	W
ATOM	4088	H1	H2O	664	26.870	24.438	7.976	1.00	0.00	W
ATOM	4089	H2	H2O	664	27.001	25.582	6.969	1.00	0.00	W
ATOM	4090	OH2	H2O	665	27.337	30.554	12.167	1.00	49.69	W
ATOM	4091	H1	H2O	665	27.488	30.006	11.008	1.00	0.00	W
ATOM	4092	H2	H2O	665	27.948	31.016	11.438	1.00	0.00	W
ATOM	4093	OH2	H2O	666	46.015	32.197	10.179	1.00	66.86	W
ATOM	4094	H1	H2O	666	46.060	31.519	9.497	1.00	0.00	W
ATOM	4095	H2	H2O	666	45.411	31.827	10.833	1.00	0.00	W
ATOM	4096	OH2	H2O	667	38.943	37.883	11.978	1.00	47.87	W
ATOM	4097	H1	H2O	667	39.367	37.487	11.188	1.00	0.00	W
ATOM	4098	H2	H2O	667	38.521	37.114	12.362	1.00	0.00	W
ATOM	4099	OH2	H2O	671	33.437	58.101	2.269	1.00	46.65	W
ATOM	4100	H1	H2O	671	33.555	57.162	2.433	1.00	0.00	W
ATOM	4101	H2	H2O	671	33.962	58.514	2.961	1.00	0.00	W
ATOM	4102	OH2	H2O	672	27.551	31.314	20.022	1.00	30.15	W
ATOM	4103	H1	H2O	672	27.929	32.042	20.533	1.00	0.00	W
ATOM	4104	H2	H2O	672	26.845	31.764	19.552	1.00	0.00	W
ATOM	4105	OH2	H2O	673	25.714	36.908	21.385	1.00	36.95	W
ATOM	4106	H1	H2O	673	24.806	37.123	21.637	1.00	0.00	W
ATOM	4107	H2	H2O	673	25.599	36.284	20.654	1.00	0.00	W
ATOM	4108	OH2	H2O	674	38.244	66.897	12.076	1.00	37.36	W
ATOM	4109	H1	H2O	674	37.773	67.536	12.626	1.00	0.00	W
ATOM	4110	H2	H2O	674	38.153	66.104	12.618	1.00	0.00	W
ATOM	4111	OH2	H2O	675	35.762	36.553	-3.986	1.00	58.40	W
ATOM	4112	H1	H2O	675	35.600	37.449	-3.677	1.00	0.00	W
ATOM	4113	H2	H2O	675	35.549	36.642	-4.923	1.00	0.00	W
ATOM	4114	OH2	H2O	676	30.689	32.814	25.675	1.00	59.30	W
ATOM	4115	H1	H2O	676	30.093	32.571	25.880	1.00	0.00	W
ATOM	4116	H2	H2O	676	31.550	33.214	25.540	1.00	0.00	W
ATOM										BND

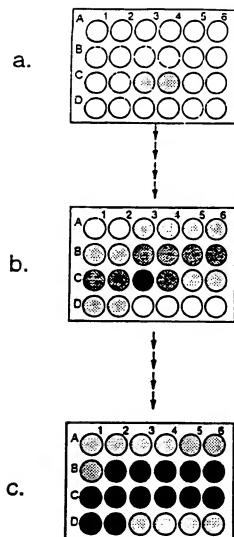


FIGURE 6



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Application Number
EP 94 10 1207

DOCUMENTS CONSIDERED TO BE RELEVANT			
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P, X	PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA vol. 90, June 1993, WASHINGTON US pages 5167 - 5171 C.P. HILL ET AL 'The structure of Granulocyte-colony-stimulating factor and its relationship to other growth factors' * the whole document *	1-8	
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X	WO-A-87 01132 (KIRIN-AMGEN, INC.) * claims; examples 7-9 *	9	TECHNICAL FIELDS SEARCHED (Int.Cl.8) C12N C07K C12P
D	& US-A-4 810 643 (KIRIN AMGEN, INC.) 7 March 1989		
X	WO-A-89 05824 (GENETICS INSTITUTE, INC.) * the whole document especially page 17 table 2, page 21 lines 16-19 and page 22 lines 25-37 *	17-22	
D	& US-A-4 904 584 (GENETICS INSTITUTE) ----- -/--		
The present search report has been drawn up for all claims			
Place of search		Date of completion of the search	Examiner
THE HAGUE		11 May 1994	Le Cornec, N
CATEGORY OF CITED DOCUMENTS			
<p>X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document</p> <p>T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document</p>			



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Application Number
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DOCUMENTS CONSIDERED TO BE RELEVANT			
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A,D	BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS vol. 159, no. 1, 28 February 1989, DULUTH, MINNESOTA US pages 103 - 111 TETSURO KUGA ET AL 'Mutagenesis of human granulocyte colony stimulating factor' * the whole document *	9-60	
D,Y	EP-A-0 344 796 (CHUGAI SEIYAKU KABUSHIKI KAISHA) * the whole document *	1-8	
Y	BIOCHEMISTRY vol. 30, 1991, EASTON, PA US pages 4151 - 4159 L. ABRAHMSSEN ET AL 'Engineering subtilisin and its substrates for efficient ligation of peptide bonds in aqueous solution' * the whole document especially page 4152 right column, page 4153 right column and the discussion *	1-8	
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P,A	WO-A-93 25687 (CHIRON CORPORATION) * page 16, line 11 - page 17, line 5 * * examples 1,9,10,11,13 * * appendix 1 * * claims *	1-8	
<div style="text-align: center;">--- -/-</div>			
The present search report has been drawn up for all claims			
Place of search THE HAGUE		Date of completion of the search 11 May 1994	Examiner Le Corneec, N
CATEGORY OF CITED DOCUMENTS X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background P : non-written disclosure I : intermediate document T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons A : number of the same patent family, corresponding document			



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Application Number
EP 94 10 1207

DOCUMENTS CONSIDERED TO BE RELEVANT			Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cls.)
Category	Citation of document with indication, where appropriate, of relevant passages			
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A	EP-A-0 456 200 (BOEHRINGER MANNHEIM GMBH) ---			
D, A	JOURNAL OF APPLIED CRYSTALLOGRAPHY vol. 20, 1987 pages 366 - 373 M.J. COX ET AL 'Experiments with automated protein crystallization' ---			
T	POUR LA SCIENCE vol. 183, January 1993 pages 76 - 82 A. OLSON ET AL 'Voir les Molécules biologiques' ---			
Y	PROTEIN ENGINEERING 1987, ALAN R. LISS, INC. pages 35 - 44 M. KARPLUS 'The prediction and Analysis of mutant strutures' * the whole document *	1-8		
A	WO-A-88 01775 (GENEX CORPORATION) 10 March 1988 -----			
The present search report has been drawn up for all claims				
Place of search		Date of completion of the search	Examiner	
THE HAGUE		11 May 1994	Le Cornec, N	
CATEGORY OF CITED DOCUMENTS				
<p>X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document</p> <p>T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons @ : number of the same patent family, corresponding document</p>				